SURGICAL LESIONS OF THE FACIAL NERVE: WITH COMMENTS ON ITS ANATOMY

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SURGICAL LESIONS of the facial nerve are nearly always due to trauma, but there is a smaller group of patients who require operation upon the nerve because of intractable facial spasm. The main purpose of treatment in both of these surgical affections of the nerve is to correct a conspicuous facial deformity. While facial paralysis and intractable facial spasm both produce embarrassing facial deformities, the spasm, being a deformity in motion, is the more conspicuous of the two.

Trauma of the nerve trunk almost invariably causes paralysis involving the entire facial musculature. In a paper before this Association in 1939, an effort was made by the writer to analyze the facial deformity due to paralysis of the trunk of the nerve. The components of the deformity mentioned at that time will be emphasized on the basis of further observations.

The massive facial deformity resulting from paralysis of the trunk of the nerve is not uniformly distributed. It is less obvious in the upper facial area and reaches its maximum about the mouth. The most conspicuous and embarrassing feature of the deformity of unilateral facial paralysis arises from displacement of the mouth by unopposed contraction of the muscles of the healthy side, whereas the alteration of facial appearance caused by paralysis of other muscle groups, such as those of the cheek, eyelids, and brow, is not exaggerated by activity of the muscles on the normal side. In long continued facial paralysis there is inevitable sagging of the angle of the mouth, causing the lips to assume an oblique direction. The result is a repulsive deformity (Fig. 1). Paralysis of the lower muscle groups supplied principally by the mandibular division permits deviation of the mouth to the opposite side, causing a sudden increase in the deformity when the healthy side of the face goes into action. The musculature in the upper half of the face is more or less fixed to its own side and is comparatively unaffected by muscle action of the opposite side. Not only is the deformity of facial paralysis greater about the lower face

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and mouth, but the permanent residuals of such paralysis after reinnervation of the previously paralyzed muscles are most noticeable in this area regardless of the type of surgical procedure employed for restoration of function. Balance of the mouth is maintained principally by action of the mandibular branch which should be regarded as the most important single branch of the nerve in the preservation of facial symmetry.

Protection of the facial nerve from injury during certain operations for lesions in close proximity to the nerve may be more difficult and a matter of more concern than the surgical treatment of the nerve, itself, for paralysis. Injury to the nerve during such operations, with resulting paralysis, however unavoidable, causes a serious deformity to the patient and must

A   B
Treatment of Facial Paralysis With Fascial Strips

FIG. 1.—(A) Characteristic appearance of patient with facial paralysis of long standing. Paralysis followed complete removal of a left acoustic neurinoma. The sagging of the face and drooping of the angle of the mouth are the conspicuous features of the deformity. The facial muscles had lost galvanic response and anastomosis was not indicated. The patient's serious condition following operation precluded early anastomosis of the nerve, which is desirable within a few weeks after removal of the tumor.

(B) Appearance of patient after support of the paralyzed side by subcutaneous fascial strips anchoring the muscles about the mouth to the temporal muscle, after the method of Brown. Small fascial strips also were used to support the lower eyelid.

be considered a severe penalty for the patient to pay for a surgical procedure. Malignant lesions lying in the course of the nerve, such as tumors of the parotid, may require sacrifice of the nerve to eradicate the lesion; but even in such cases the patient should be told in advance of the likelihood of facial paralysis with careful explanations as to what such paralysis really means. The protection of the facial nerve in the removal of malignant conditions which have not actually invaded the nerve requires a thorough knowledge of the nerve anatomy and its branches and the use of a technic which exposes the nerve adequately so that removal of the lesion may be accomplished with the nerve clearly visualized.

The facial nerve may be jeopardized in varying degrees by the following operations: Complete removal of acoustic neurinomas; section of the auditory nerve for Ménière's disease or intermediate nerve for certain paroxysmal neuralgias; temporal or suboccipital section of the root of the gasserian ganglion for tic douloureux; mastoidectomy; and removal of extracranial tumors, such as those of the parotid.

Operation may be required to relieve paralysis resulting from injury to any part of the nerve trunk or its main peripheral branches. The branches of the nerve are frequently divided by stab wounds and spicules of glass in the region of the parotid. In such cases the mandibular branch usually escapes injury, being protected by the ramus of the jaw (Fig. 2).

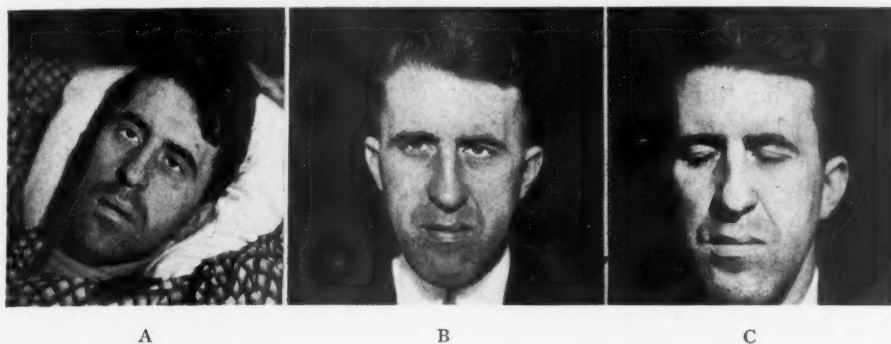A   B   C

FIG. 2.—(A) Patient with bilateral paralysis of the sixth and seventh nerves from fracture of the base of the skull. The right facial and both sixth nerves recovered in about six months but there was no improvement in the left facial at the end of 12 months. A faciohypglossal anastomosis was then performed on the left side.
(B) Appearance of patient one year after faciohypoglossal anastomosis on the left.
(C) Patient shown in (A) and (B), two and one-half years after anastomosis. Mass movements in this case were not pronounced.

Intracranial injuries of the nerve nearly always result from complete removal of an acoustic neurinoma. In recent years in my clinic this has been the cause of a large majority of cases of division of the trunk, injury from mastoid operations having become much less frequent due to more expert surgery. Destruction of the facial nerve intracranially has been generally accepted in this country as an almost inevitable penalty the patient must pay for complete removal of the average size acoustic neurinoma, although some of the smaller tumors may be removed without serious damage to the nerve. In the writer's experience, one of the largest acoustic neurinomas in the series was completely removed without severing the nerve, but we have not been able to duplicate this rather fortunate experience. If damage to the facial nerve could be prevented in the formidable operation for complete removal of these tumors, the procedure would represent one of the most brilliant technical achievements. Perhaps this may yet be accomplished and Olivecrona's success in removing these tumors completely without dividing the facial nerve should certainly stimulate greater efforts by other surgeons toward protection of the nerve in this important operation.

Direct injury to the facial nerve in section of the auditory for Ménière's disease can nearly always be avoided if one has a good knowledge of the local anatomy. There may be a delayed and temporary paralysis following operation, probably due to edema. Division of the intermediate nerve without injury to the facial is more difficult, but the problem here is by no means so complicated as that involving large acoustic neurinomas. Furlow has reported a very interesting case of section of the intermediate nerve for intractable neuralgia without damage to the facial nerve.

The facial nerve is temporarily paralyzed in a small percentage of cases in temporal section of the sensory root of the gasserian ganglion for tic douloureux. There is rather general agreement at the present time that the cause of this paralysis is traction on the superficial petrosal nerve which leaves the facial from the geniculate ganglion. Such traction causes injury and edema of the facial with resulting paralysis for some weeks or months. In elevating the temporal dura for exposure of the sensory root, the superficial petrosal should be avoided, and if this is impossible, it should be sectioned to prevent the possibility of traction on it.

We have adopted a conservative attitude toward facial paralysis following mastoid operations and have allowed at least six months for signs of spontaneous recovery unless the otologist were positive the nerve had been severely damaged. We have also adopted a conservative attitude in the treatment of facial paralysis following fracture of the base of the skull in view of the large percentage of cases of spontaneous recovery (Fig. 3).

The removal of extracranial tumors along the course of the nerve, particularly those that lie deep in the digastric fossa, may seriously menace the nerve. In these tumors, as in other large tumors about the parotid, we have followed a plan of exposing the branches of the nerve distal to the parotid and tracing them backward to the pes anserina, then exposing the trunk before attacking the tumor, itself. Damage to the nerve in the extirpation of these tumors, in the writer's experience, is most likely to occur to the mandibular branch, and we believe it is most important to isolate this branch at a point where the facial artery crosses the mandible and trace it backward to the trunk before the tumor is removed.

The type of surgical treatment for the relief of facial paralysis obviously will depend upon the location of the injury. When the nerve is divided intracranially, as in the complete removal of acoustic neurinomas, reinnervation of the facial muscles can be accomplished in only one way, that is, by the substitution of a healthy motor cranial nerve for the proximal portion of the facial. The nerve selected for the purpose of anastomosis usually has been either the hypoglossal or the spinal accessory, depending on the choice of the individual operator. In the selection of a nerve for anastomosis with the facial, one must give consideration not only to the functional results expected from the anastomosis, but to the disability resulting from sacrifice of the nerve to be used to replace the facial. In nearly all cases we have utilized the hypoglossal for fusion with the paralyzed facial,

not only because of the functional similarity of the two nerves, but because
the sacrifice of the hypoglossal nerve in our cases has produced no appreciable
loss of important function. Careful voice studies before and after operation
have shown no change in voice which could be attributed to the loss of the
hypoglossal nerve. We have seen no case in which disturbance of deglutition
was more than a temporary complaint. The spinal accessory nerve has been

FIG. 3.—(A) Division of the upper branch of the right facial
nerve by a fragment of glass. The uninjured mandibular branch of the
facial maintains balance of the face.

(B) Sketch shows location of lesion. This is a common site of
injury to the nerve. The mandibular branch generally escapes, being
protected by the ramus of the jaw.

(C) Appearance of patient four years after suture of the upper
branch. The wound was infected on admission to the hospital and
suture was delayed for several weeks. The patient's facial appearance
is normal; the corrugator muscles recovered, but there was no return
of frontalis function.

(D) Patient, shown in (A), (B) and (C) is able to close the
eyes without mass movements.

used in only a few cases and then because of some special objection to dividing
the hypoglossal. Further observations on injury to the spinal accessory nerve
have confirmed earlier impressions that section of this nerve may constitute
a disability of some importance, but varying in severity in individual cases.

Spinal accessory paralysis has been studied recently with a great deal of thoroughness by Major Barnes Woodhall at the Ashford General Hospital. Major Woodhall states in a recent communication that "section of the spinal accessory nerve is certainly a disabling injury in military service" and that "the disability was not compatible with full military duty."

Facial anastomosis with either the hypoglossal or spinal accessory will restore motion to the paralyzed muscles, but there are mass movements of the face which is likewise true after suture or graft of any part of the nerve trunk. The results of anastomosis are also marred to some extent by associated movements which vary considerably in individual patients. In loquacious patients and those in which the tongue is brought into more active use in chewing and swallowing, the associated movements may be very much exaggerated. The results of anastomosis might be improved by careful individualization of patients in the selection between the hypoglossal and the spinal accessory, using the latter for the vivacious type and the hypoglossal for those who use the tongue less freely.

A careful appraisal of the results of anastomosis of the facial with another motor cranial nerve shows that while there is great improvement in the facial appearance, normal facial activity is never restored. In repose, the patient's appearance is practically normal, there being no atrophy of the facial muscles, no asymmetry, and no sagging of the lower face. However, emotional expression never returns to the paralyzed side although the patient by deliberate effort may acquire a poor imitation of normal facial expression. Under the stimulus of emotion, the normal side moves much more rapidly and spontaneously so that the mouth is drawn to the healthy side. Restoration of function of the frontalis muscle has not been observed by the writer after anastomosis except in one case, and in this instance the hypoglossal was used. I know of no satisfactory explanation for the failure of this muscle to recover movement after severe disease or injury of the nerve trunk. So far we have seen no return of platysma function following either suture or anastomosis of the facial nerve.

Injury of the nerve trunk in the facial canal, usually produced by operation upon the mastoid, has been repaired by short nerve grafts, according to the method of Ballance and Duel. The most difficult part of this operation is the exposure of the facial canal and segments of the nerve in the diseased mastoid. To do this expertly requires special training in mastoid technic. The application of the nerve graft in such cases after exposure of the injured facial nerve is a relatively simple procedure.

Suture or graft of the nerve when practicable is preferred to any form of anastomosis, not because of better functional results, but because associated movements do not develop nor does the operation require the sacrifice of any other nerve. Insofar as restoration of facial movement and symmetry are concerned, the anastomosis is as effective as suture or graft of the trunk.

Repair of the facial trunk when it is severed extracranially by a stab wound is not difficult if it is done at the time the wound receives primary
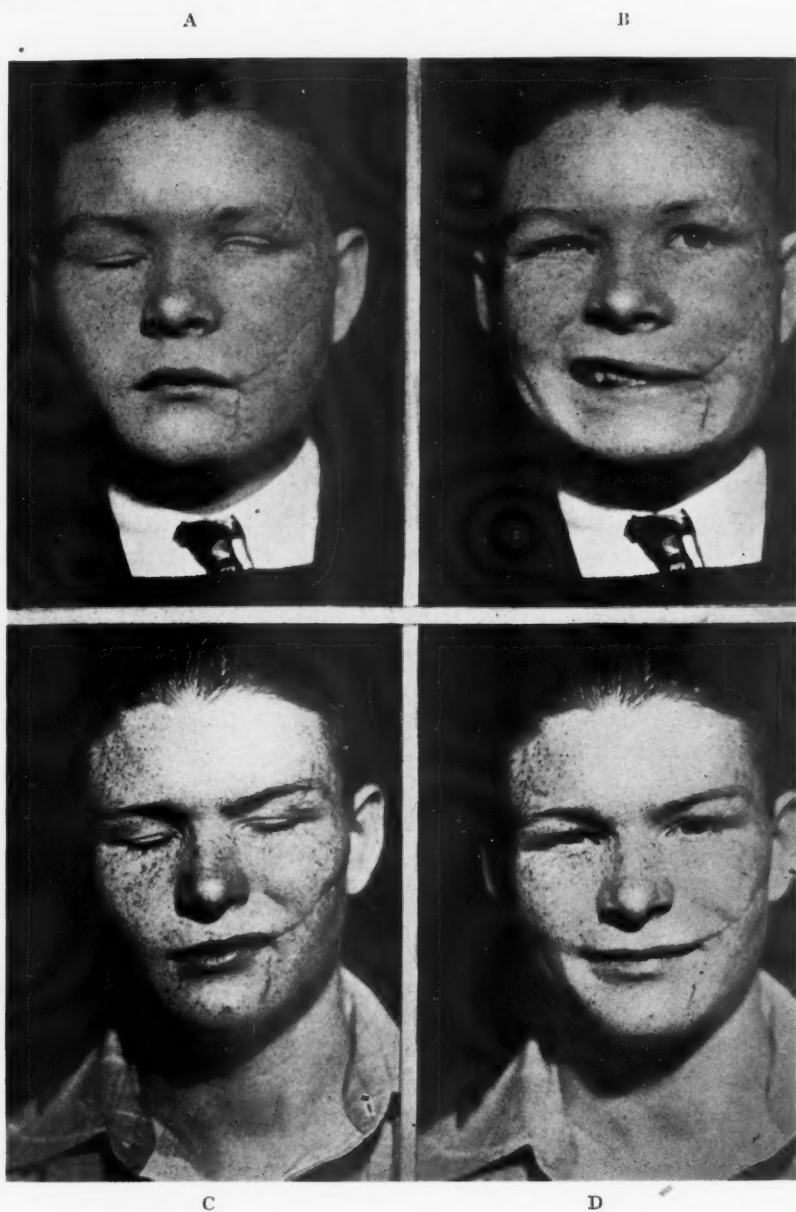
A B

C D

FIG. 4.—(A and B) Division of the upper and middle branches of the facial nerve by glass. Balance of the mouth is retained in repose but there is marked asymmetry on attempts to show the teeth. Patient is unable to close his eye. No effort had been made to suture the nerve at the time of primary treatment of the wound.

(C and D) Patient shown in (A and B), eight months after suture of the upper and middle branches. The patient is able to close his eyes without mass movements and his mouth is balanced in smiling.

treatment. The same is true of the important branches of the nerve. If operation upon the nerve is delayed, formation of scar tissue makes the exposure and identification of the nerve or its branches much more difficult. It is almost incredible that patients with an incised or penetrating wound in the region of the parotid, who are unable to close the eye or retract the angle of the mouth on the injured side, should have the skin wound sutured without any effort being made to expose and repair the nerve which is always divided (Fig. 4). There is no other explanation for paralysis following immediately a stab wound along the course of any motor nerve, yet the patient is often told the nerve was traumatized and that spontaneous recovery may take place. If the divided nerve is repaired at the time primary treatment is given the wound, its identification may be facilitated by the faradic electrode, whereas if there is a few days' delay, the distal segment of the nerve loses faradic response, and a more extensive dissection is required.

The facial nerve may be injured and considerable loss of nerve substance result from gunshot wounds. If the injury is located in the region of the pes anserina, repair of the nerve lesion is often possible only by grafts. With wide destruction of the nerve branches, support of the face on the paralyzed side by fascial strips is the treatment indicated. Injury of the nerve by gunshot in the region of the mastoid was occasionally seen in cases of the last war. These injuries often cause extensive nerve destruction and reinnervation can be brought about only by anastomosis of the facial with another healthy motor cranial nerve.

The technic of facial anastomosis and suture has been previously described in considerable detail and need not be discussed further. In the repair of certain important peripheral branches of the nerve, technical difficulties may be encountered. It may be necessary at times to suture the trunk of the nerve to two or more of its peripheral branches. We have found this difficult in some cases particularly when the mandibular branch as well as those to the eye and cheek require approximation to the trunk. To overcome the difficulty here presented, we have felt that a combination of suture and the plasma cuff of Mediwar and Young might be helpful in some of these cases. In one instance of division of the trunk and its main branch during removal of a malignant tumor, and suture of the three main branches to the trunk being impossible, the two upper divisions were sutured to the trunk and an anastomosis of the spinal accessory with the mandibular branch was done. The results were very satisfactory (Fig. 5). In another case, suture of the branches to the eye and cheek was supplemented by a fascial strip to the mouth attached to the temporal muscle after Brown's method. The results here were excellent (Fig. 6). In all cases of suture we have used arterial silk for approximating the epineurium of the trunk and one carefully placed through-and-through suture for the small branches.

The facial nerve has great capacity for regeneration under any but the most unfavorable conditions, but mass movements always occur following regeneration. This is true whether there has been division of the trunk

or of one or more of its branches, but in the latter case, the mass movements are confined to one group of muscles and are less conspicuous. In explanation of this, Howe, Tower and Duel, Ford and Woodhall, and others, have found that after section of the nerve or a severe degenerative lesion, regenerating

A   B

Suture of facial trunk to
upper branches of nerve

C   D   E

FIG. 5.—(A) Right facial paralysis following removal of a large malignant tumor of the parotid. The tumor extended deeply into the digastric fossa. The mandibular branch was involved in the tumor and a portion of this branch was sacrificed. The nerve trunk was much elongated. A portion of this was excised and the trunk was sutured to the upper and middle branches. It was impossible to make satisfactory suture of the mandibular branch to the trunk. Because of the importance of this branch it was anastomosed to the spinal accessory, the patient preferring the use of the latter nerve in the anastomosis. The case illustrates the difficulty of suturing the three main branches of the nerve to the trunk. This difficulty arises from the marked divergence of the mandibular from the other two main branches.

(B) Sketch of operation described in Figure 5 (A). When direct suture of the mandibular branch to the trunk is impossible, anastomosis of this branch with either the hypoglossal or spinal accessory is indicated.

(C), (D) and (E) Patient in Figure 5 (A), eight months after operation. The face is balanced in repose, there is ability to close the eye without conspicuous mass movements, and in smiling there is only slight deformity of the mouth.

fibers normally intended for one group of muscles may penetrate every muscle group within the facial domain. The result is that when the patient attempts to close his eye, the muscles about the mouth contract while efforts to move the lips are associated with contraction of the orbicularis oculi

A   B   C

Combination of Nerve Suture and Fascial Strips in the Treatment of Facial Paralysis.

FIG. 6.—(A) Injury of the left facial nerve in operation for extensive osteomyelitis of the jaw. It was possible to suture the upper branches to the trunk. These branches evidently sent some supply to the upper lip. Suture of the mandibular branch was impossible. Strips of fascia lata, after Brown's method, were used to support the upper and lower lips. Photograph one year after operation. Recovery of orbicularis function has begun. The mouth is well balanced.

(B) Photograph of patient shown in Figure 6 (A), three years after operation. He is able to close his eye, his face is balanced and there has been some recovery of muscle function of the upper lip. Symmetry of the lower face is well preserved by the fascial strips.

(C) Patient is able to close eyes without mass movements.

A   B

FIG. 7.—(A) Mass movements following recovery of function after division of the trunk of the facial nerve proximal to the parotid gland by a splinter of wood following direct nerve suture. Patient has restoration of all muscle groups except the frontalis. There are mass movements in attempts to close the eye. The case illustrates the inevitable development of mass movements following division of any portion of the facial trunk.

(B) Patient in Figure 7 (A) shown in repose.

(Fig. 7). This phenomenon of faulty regeneration partly explains the failure of any surgical procedure to restore normal movements or emotional expression to the face following severe lesions of the nerve trunk. Much has been said about reeducation of the patient after suture, graft or anastomosis of the facial nerve, but it is difficult to understand how such reeducation could be helpful when the muscles of expression have been converted by faulty nerve regeneration into a functional unit incapable of dissociated action of the various muscle groups which is so essential to normal facial expression. It is much more logical to impress the patient with the importance of repression

A   B   C

FIG. 8.—(A) Severe intractable facial spasm. Section and suture of the upper branches of the nerve had been carried out twice, with relief of the spasm for about six months following each operation. In the meantime the spasm had spread to the lower facial muscles, producing a very conspicuous and embarrassing deformity. The patient was greatly handicapped in her work as a teacher and requested the radical operation.

(B) Patient shown in Figure 8 (A), 11 months after division of the trunk of the facial nerve and anastomosis with the hypoglossal. The photograph shows the face well balanced and serene.

(C) The mouth is fairly well balanced in attempting to smile. The maximum recovery of function following anastomosis has not been reached and complete closure of the eye was not possible at the time the photograph was made but muscle tone about the eye is evident. Recovery of frontalis function is not expected and the penalty for this is slight lowering of the eyebrow.

of all facial activity since the residuals of the former paralysis are not noticeable when the face is in repose.

A brief reference only will be made to facial spasm. The subject was discussed before this Association in a previous paper. Inasmuch as the involuntary contraction of the orbicularis oculi muscle is the most disturbing feature of intractable facial spasm, the nerve supply to this muscle is sectioned and resutured as a primary treatment. This operation may be compared to alcohol injection of a branch of the fifth nerve for the temporary relief of tic douloureux. The spasm usually returns in about six months, but in the meantime the patient not only has been relieved of spasm, but is in better position to know whether he wishes a more radical operation for permanent cure. We have never had a patient complain of facial paralysis produced in an effort to relieve facial spasm.

Severe facial spasm gives a patient such a grotesque appearance that he is willing to pay almost any penalty for its relief. If the spasm is confined

chiefly to the orbicularis oculi, and particularly if it recurs after previous section and suture of the nerve, this branch may be resectioned and the course of the proximal segment so changed as to prevent regeneration. However, if the spasm involves practically all the facial muscles, as is often the case, section of the nerve with faciohypoglossal anastomosis is recommended with full explanations to the patient as to this procedure in all its details (Fig. 8).

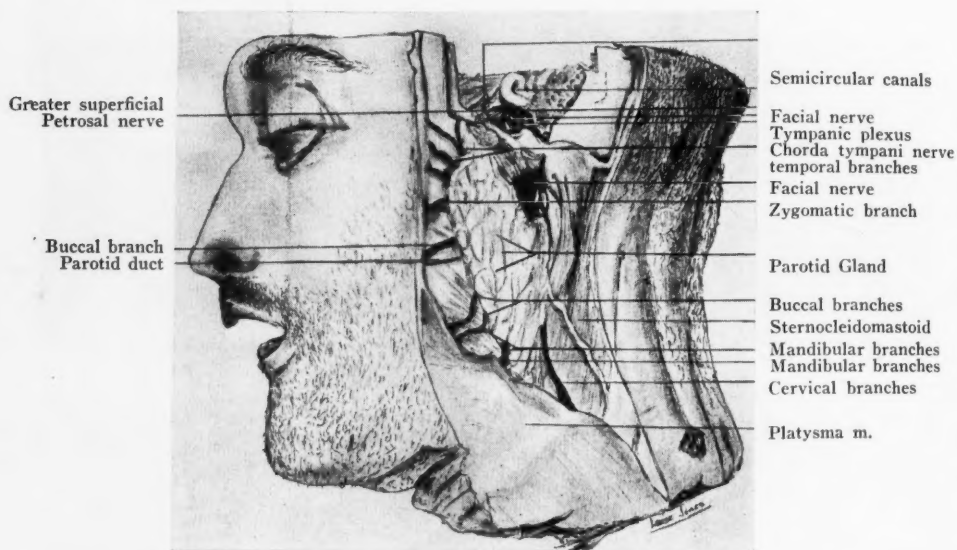Facial spasm is rarely bilateral, although we have seen a number of such

FIG. 9.—Drawing from actual dissection of the left facial nerve. The main branches of the nerve may be found after their emergence from the parotid gland. These branches may be easily identified at this point and traced back to the trunk or to the site of injury. In removal of certain parotid tumors, exposure of the nerve anterior to the gland provides protection to the nerve by keeping it in full view during removal of the tumor.

cases, due probably to encephalitis. Bilateral facial spasm produces not only a most conspicuous deformity, but also a marked disability. The patient may become helpless in traffic; unfit for driving a car; endangered in going down steps; and greatly handicapped in numerous ways by violent contraction which forcibly closes the eyes. In bilateral facial spasm practically the whole facial musculature, including the platysma, is involved. In the treatment of this condition we section the facial trunk and perform an anastomosis with the hypoglossal on the side most involved. The branches to the eye on the opposite side are sectioned and measures taken to prevent regeneration. Sagging of the lower lid after permanent paralysis of the orbicularis oculi can be improved by external canthoplasty or facial strip support.

In a number of dissections of the facial nerve prepared in Department of Anatomy of the Medical College of Virginia, we have been impressed

with the complexity and variation of the nerve pattern (Fig. 9).*   In some
patients the nerve begins to break into its main branches before the mandible
is reached and there may be a second redistribution of the branches, resembling
the pes anserina.   The sketches of the facial nerve in text books give a very
incomplete and inaccurate picture of the facial nerve as revealed in minute
dissections (Fig. 10).*   While there are three main groups of branches to
supply the eye and forehead, the cheek, the lower lip and neck, there appears
to be an intricate anastomosis of all these various branches so that fibers
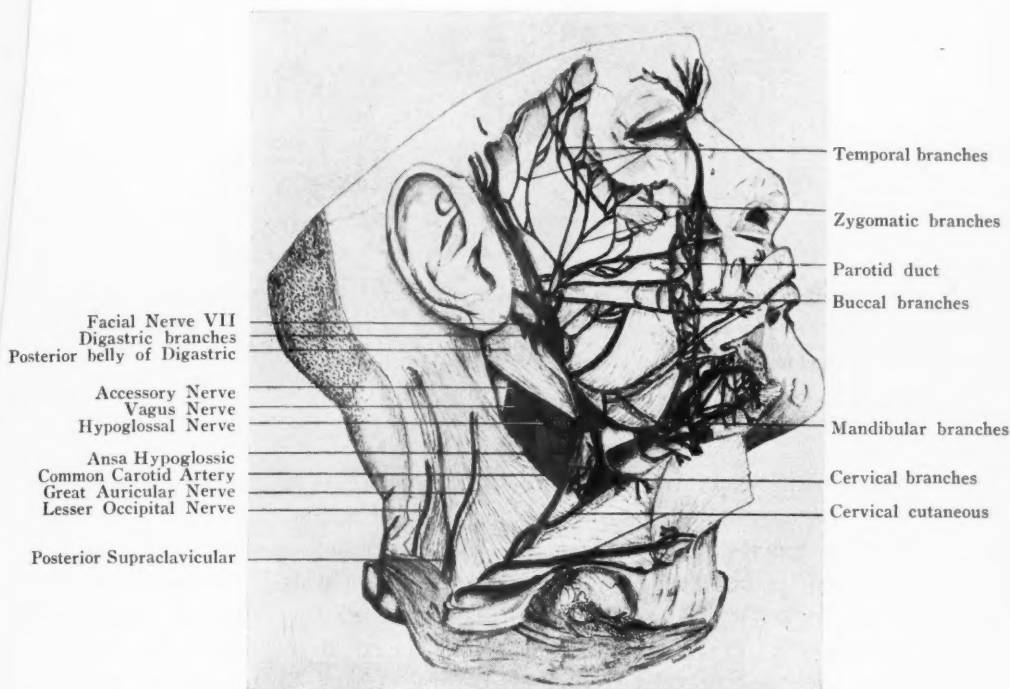

Fig. 10.—Drawing shows minute dissection of the facial nerve. The parotid gland has been removed. There is wide variation in the nerve pattern but there is a consistent tendency to three plexus-like arrangements in the three main divisions. The plexus of the mandibular branch is usually the most complex of the three. There seems to be a tendency for the nerve branches to avoid a space overlying the masseter muscle. The digastric branches are well shown. These are important in the identification of the trunk of the nerve in the operation for anastomosis. Gentle retraction downward on the digastric muscle will expose one of these branches which may be followed to the trunk with minimal dissection. Because of the plexus-like arrangement of the nerve and the free anastomosis between the branches there may be considerable difference in the effects of lesions of similar location.

apparently destined for one group of branches may find a distribution in a
remote group. (Fig. 11).*   This very complicated arrangement of the
nerve pattern and the free anastomosis between the various groups as well
as individual branches may explain in part the difference between emotional
expression and ordinary facial movement.

*Figures 9, 10 and 11 are reproduced from drawings made at dissections in the
Department of Anatomy, Medical College of Virginia, by Mrs. Louise Jones.

Superficial Temporal artery

Semi-circular canals

Chorda tympani nerve
External auditory meatus
Facial nerve
Posterior facial vein

Digastric branches

Posterior belly of digastric

Temporal branches

Zygomatic branches

Buccal branches
Parotid duct

Mandibular branches
External maxillary artery

Cervical branches

FIG. 11.—Drawing from actual dissection shows a complicated pattern of the nerve in the portion just distal to the facial canal. Several important branches arise from the trunk at this point and division of the branches at the border of the mandible would be much more difficult to repair than a lesion in the same location in the nerve as shown in Figure 10. In this particular dissection the plexus-like arrangement of the distal branches is much less complicated.

CONCLUSIONS

The limitations to complete success of surgery of the facial nerve are obvious and apparently insurmountable. The principal cause of imperfect recovery of function after division of the nerve trunk appears to be faulty regeneration of the nerve. Whether the lesion is paralysis of the nerve or facial spasm for which paralysis must be produced for relief, the purpose of operation is to remove a conspicuous facial deformity. The facial muscles, once disconnected from their central control by trauma or severe disease of the nerve trunk, never recover the power of normal emotional expression. Motility can be restored to the paralyzed face by direct suture, nerve graft or anastomosis, depending on the type of case. Notwithstanding the permanent loss of emotional expression on the previously paralyzed side, great improvement is obtained by restoring facial symmetry, preventing atrophy, and protecting the eye. The results of surgery for facial nerve lesions are by no means perfect but it is possible to relieve a very depressing facial deformity by appropriate operative procedures.

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DIVERTICULA OF THE URINARY BLADDER*

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INCIDENCE

Diverticulum of the urinary bladder is a complication of clinical importance in about 6 per cent of cases of obstruction at the vesical neck. Most of these are encountered in men between the ages of 50 and 70, with benign prostatic hypertrophy. The smaller incidence in men with carcinoma of the prostate can be explained by the fact that the period of obstruction is shortened by the life expectancy of carcinoma patients. The early spread of carcinoma of the prostate through the capsule and into the periprostatic region also lessens the degree of obstruction in these cases as compared with benign hypertrophy where the growth is confined to the capsule. The occasional cases occurring in children are usually associated with congenital lesions such as prostatic valves and contractures of the vesical neck. Scar tissue resulting from inflammatory conditions of the bladder and urethra is considered responsible for the small number of cases in females.

ETIOLOGY

Whether diverticulosis of the bladder is congenital or acquired is of little more than academic interest. Congenitally weak spots exist in the retrotrigonal region and the posterolateral walls near the ureteral orifices and the site of the urachus. These constitute what Kimbrough[1] termed factors of "soil preparation" always present in the vesical wall. Certainly, in the routine management of urologic patients one is impressed by the apparent immunity of the majority of bladders to the development of diverticula. Congenital obstruction at the neck of the bladder in children often progresses to the point of complete decompensation of the upper urinary tract without the formation of a diverticulum (Fig. 1). However, in another child similarly obstructed for the same period of time a diverticulum will form (Fig. 2). Acquired obstruction in adults shows an absence of this complication in approximately 95 per cent of cases. Thompson[2] and others have called attention to the fact that in cases in which diverticula do develop, the frequent association of other conditions, such as inguinal and diaphragmatic hernia, indicates a congenital weakness of tissue.

FIG. 1   FIG. 2

FIG. 1.—Complete congenital obstruction at neck of bladder in child, age 5, without diverticulosis.
FIG. 2.—Complete congenital obstruction at neck of bladder in child, age 5, with diverticulosis.

FIG. 3a   FIG. 3b

FIG. 3a.—Diverticulum with large orifice and sufficient contractile ability to empty, which produced
no symptoms.
FIG. 3b.—Postoperative cystogram one month after operation (transurethral resection).

SYMPTOMS

There are no pathognomonic symptoms of vesical diverticula. Difficulty
in urination, frequency, pain, hematuria, pyuria, incontinence and retention
are frequent complaints. These are also symptoms of obstruction at the
neck of the bladder and would not necessarily suggest the presence of a
diverticulum. The so-called installment urination may be regarded as

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presumptive evidence. . In such cases the patient passes a small amount of urine and a few moments later a larger amount which may be extremely cloudy. Many of these pouches produce no trouble during life and are discovered only at autopsy. In these cases the opening of the diverticulum is usually large and the wall of the sac has sufficient contractile ability to

FIG. 4 FIG. 5
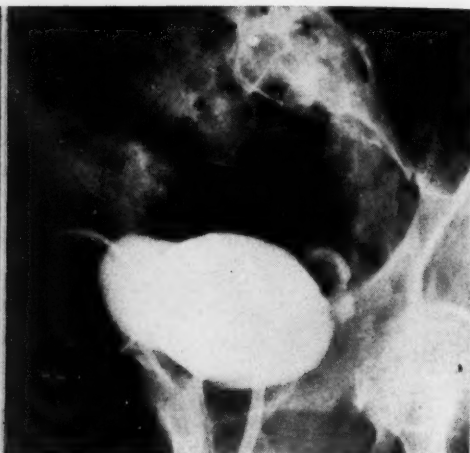FIG. 4.—Infiltrating growth which has spread to bladder wall.
FIG. 5.—Papillary growth which can be seen through the wide orifice of a shallow sac.

empty, thereby reducing the possibility of infection, the chief source of symptoms (Fig. 3a and 3b).

COMPLICATIONS

The complications of vesical diverticula are (1) infection; (2) stone formation; (3) tumor; (4) hemorrhage; (5) damage to the corresponding ureter; and (6) rarely rupture.

Infection is the most common complication of a diverticulum which does not completely empty itself. A weak wall of the sac and a narrow orifice through which it communicates with the bladder favor the development and persistence of infection once it has been established. In cases of long standing the infection may spread beyond the diverticulum to form dense adhesions to the surrounding structures.

Stones are found in about 12 per cent of diverticula of the bladder. A few of these may migrate into the sac from the bladder and kidneys. Those that form in the sac are probably the result of infection. This is especially true if the infection is caused by urea-splitting organisms which favor the precipitation of insoluble earthy phosphates.

Neoplasms found in vesical diverticula are of the same type that invade the bladder. They are not common, only 40 cases having been reported by 1932. Others have appeared in the literature since that time. We have

seen three cases, two of which were infiltrating and had spread to the bladder wall (Fig. 4). The other was a papillary growth which could be seen through the wide orifice of a shallow sac (Fig. 5).

Hemorrhage, unless profuse, is not necessarily a complication but may be regarded as a symptom of some other condition in the diverticulum.

The corresponding ureter may be damaged by the presence of a vesical pouch in one of two ways. A ureter opening into an infected sac favors ascending infection to the kidney; in addition, the diverticulum may be of sufficient size to produce partial obstruction to the lower end of the ureter by pressure, with dilatation of the ureter and renal pelvis above. The combination of infection and retention predisposes to calculus formation in the renal pelvis just as it does in the diverticulum. Although not common, this complication may be serious when it does occur.

Rarely does a diverticulum rupture, but it may occur when there is a sudden increase in intravesical pressure, especially if infection has rendered the wall friable. This complication assumes the same clinical importance as extravasation of urine from any other cause.

DIAGNOSIS

The diagnosis of vesical diverticula is based on a careful cystoscopic study of the bladder and roentgenologic studies of the entire urinary tract. Cystoscopy under favorable conditions offers the most accurate means of obtaining information about the bladder. On the other hand, in cases with diverticula, cystoscopy alone is not completely diagnostic. It indicates the position and size of the orifice but gives no information as to the depth and contents of the sac or the ability of the diverticulum to empty itself. It must be remembered also that nearly all of these patients are of advanced age, with prostatic obstruction and some degree of renal and cardiovascular damage. Because instrumentation in such patients is followed by an occasional serious reaction, it is our policy to complete all other studies first. This routine has enabled us to obtain sufficient information in the majority of cases from roentgenologic, and other studies, to make the indications for treatment apparent. Thus, in the majority of cases cystoscopy is not performed until the patient is anesthetized and ready for operation. An exception to this routine is made when the history, physical findings and roentgenologic studies indicate the presence of a tumor in either the bladder or diverticulum.

Roentgenologic studies of the urinary tract include a plain film of the kidneys, ureters and bladder, intravenous urograms and retrograde cystograms. The plain film may indicate a diverticulum by the presence of a suspicious shadow lateral to the bladder region (Fig. 6). It will also determine the presence or absence of stones in other parts of the urinary tract. Excretory urograms in the presence of good renal function and adequate preparation will provide accurate information regarding the condition of the kidneys and ureters. Cystograms obtained in connection with intravenous urograms,

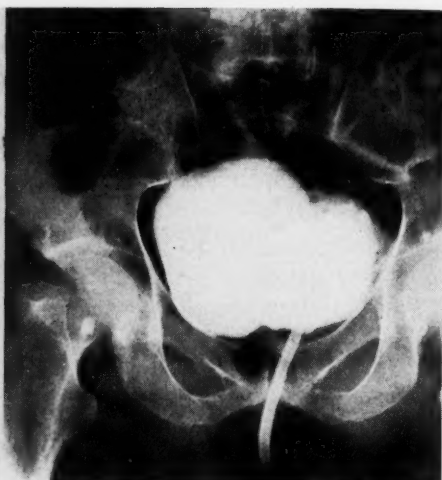FIG. 6   FIG. 7
FIG. 6.—Presence of diverticulum suggested by suspicious shadow lateral to bladder.
FIG. 7.—Retrograde cystogram showing diverticulum of bladder.

FIG. 8   FIG. 9
FIG. 8.—Anteroposterior view demonstrating diverticulum of bladder.
FIG. 9.—Lateral view showing vesical diverticulum.

are not always diagnostic, in which case retrograde cystograms are necessary (Fig. 7). Exposures are made in the anteroposterior right and left lateral positions, 5 per cent sodium iodide being used as a contrast medium. If a diverticulum is present, it is usually seen on at least two of the films (Figs. 8 and 9). A fourth exposure, made after the bladder has been emptied by catheter, will indicate whether or not the diverticulum is of the retentive type (Fig. 10). In the absence of a stone, any filling defect in the divertic-

ulum may be produced by a tumor. Cystoscopy in such cases may show the tumor projecting into the orifice. If the diverticular orifice is large, it may be possible occasionally to advance the cystoscope into the sac. Bladder spasm will sometimes defeat the purpose of both cystoscopic and cystographic studies. In such cases either intravenous pentothal or a small amount of spinal anesthetic will permit the satisfactory performance of both examinations. The importance of routine cystographic studies in all bladder neck obstructions is emphasized by the frequency with which one encounters complications from a diverticulum in these cases. Adequate studies to determine the presence and type of infection are, of course, routine.
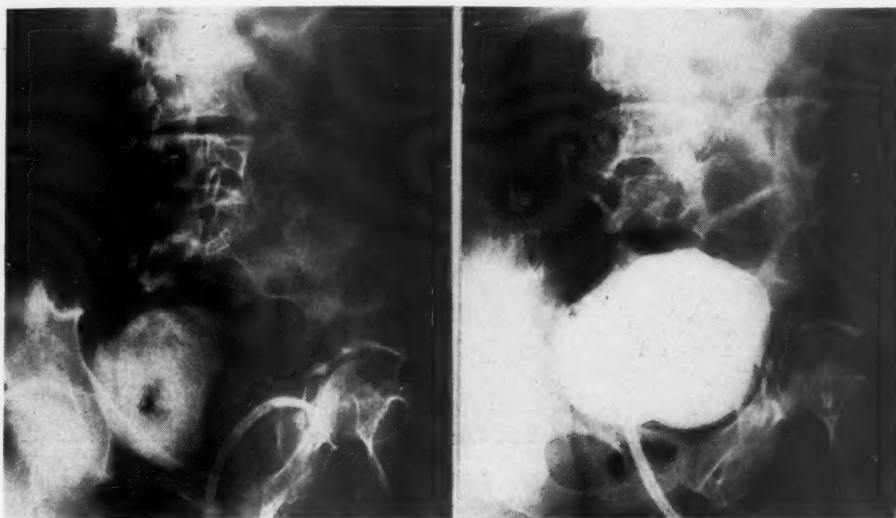

FIG. 10   FIG. 11
FIG. 10.—Cystogram made after bladder has been emptied.
FIG. 11.—Preoperative cystogram of diverticulum of bladder.

TREATMENT

The development of prostatic resection as a means of relieving prostatic obstruction has brought about a more conservative viewpoint toward the treatment of vesical diverticula. This attitude has been demonstrated by Thompson, et al.,[2] who made a comparison of cases of diverticula seen during two six-year periods at the Mayo Clinic. During the first period (1926 to 1931, inclusive) 107 diverticulectomies were performed, whereas during the second period (1932 to 1937, inclusive) there were only 30 primary and five secondary diverticulectomies, in spite of the fact that a greater number of patients were treated for bladder neck obstructions in the latter period. The size of the diverticulum alone does not constitute an indication for removal (Fig. 11). Many of these fairly large sacs with a wide orifice will contract to the point of almost complete obliteration (Fig. 12), or will produce no symptoms following removal of the obstruction at the neck of the

bladder. Diverticula with a large capacity and a narrow orifice communicating with the bladder are usually of the retentive type and require removal, particularly if they are badly infected.

Diverticulectomy should be performed in all cases with complicating stones or neoplasms with the possible exception of a small, low grade tumor where the orifice of a shallow sac is large enough to permit visualization of its cavity and destruction of the tumor with a high frequency current. There should be no question as to the grade of the tumor, however, when this procedure is performed.
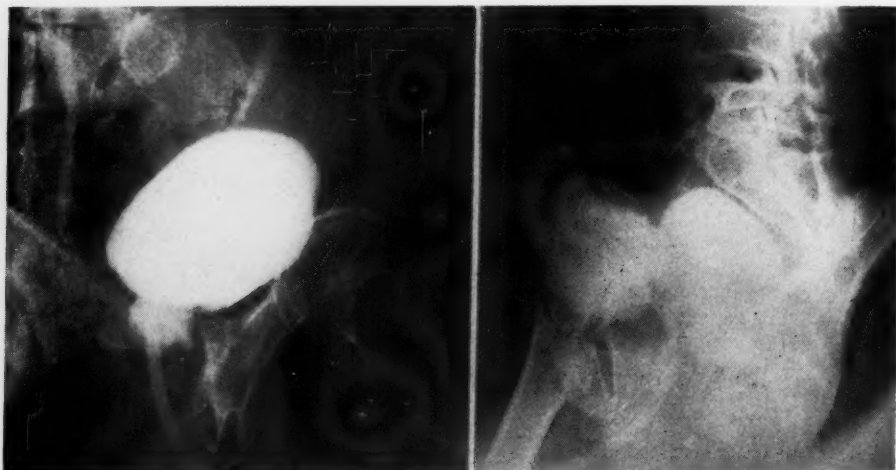

FIG. 12   FIG. 13

FIG. 12.—Postoperative cystogram of same patient.
FIG. 13.—Large diverticulum situated deep in pelvis.

Any one of several operative technics for removal of diverticula may be carried out. The extravesical dissection of the sac, as practiced by Lowsley,[3] and others, is easily performed in the case of large diverticula not attached to the surrounding structures by dense adhesions (Fig. 13). After the bladder has been incised down to the orifice, the neck of the sac may be severed from the bladder and the diverticulum removed in a retrograde manner similar to the retrograde removal of the gallbladder. This method is especially applicable in diverticula complicated by tumor. In such cases it may also be necessary to excise a portion of the adjacent vesical wall to insure complete removal of the growth. If the ureteric orifice is involved in the diverticulum, the Y-plastic, developed by Young,[4] offers a good means of preserving the normal ureteric insertion into the bladder. Reimplantation of the ureter into the bladder should be avoided if possible. Ligation of the ureter should also be avoided because of pyonephrosis which frequently develops in the kidney above necessitating nephrectomy. Occasionally, the corresponding ureter and kidney may be sufficiently damaged by dilatation and infection to necessitate an additional operative procedure. Suction of the sac into

the bladder by means of a large glass tube, also devised by Young,[4] offers a method of removing multiple diverticula in some cases. The orifice is closed and the diverticular space drained extravesically. Councill[5] recently advocated the use of a rubber balloon attached to a catheter to facilitate the intravesical removal of a diverticulum.

To remove the entire sac of a large diverticulum situated deep in the pelvis and adherent to the surrounding structures is often a tedious and time-consuming procedure. In 1939, Barnes[6] offered a simple approach to this problem which involves the principle of removing the mucous membrane from the diverticulum and leaving the remainder of the sac intact. The bladder is exposed through an adequate suprapubic incision, opened and the lateral wall incised down to the diverticular orifice. The diverticulum is then opened wide to expose its entire cavity. By means of a knife handle or dissector the mucous membrane lining is removed. If infection has been present for a long time, the mucous membrane is thickened and friable and may come away piecemeal. Barnes advocated the use of the cautery to destroy pieces of mucosa difficult to remove. The cutting-loop may also be used for this purpose. The cutting-current causes less tissue destruction than the cautery and may be used to remove the entire mucous membrane. The orifice of the diverticulum is closed after the mucous membrane has been removed. This converts the diverticulum into an extravesical pouch which is drained by a cigarette drain or Penrose tube. A cystostomy tube is left in place to divert the urinary stream. The length of time the tube is left in varies in individual cases. We have used this method in several cases in which the diverticulum was large, situated deep in the pelvis and surrounded by adhesions and in one patient with a diverticulum containing stones and frank pus (Fig. 13). It is easy to perform, rarely requires more than an hour to complete the operation and produces little more shock than simple suprapubic cystostomy.

In cases requiring removal of obstruction of the neck of the bladder in addition to diverticulectomy, it has been our routine practice to remove the diverticulum first. We can think of no reason for reversing this procedure. Thompson[2] has pointed out that transurethral resection in borderline cases does not seriously complicate the performance of diverticulectomy if this is later found to be necessary. An increased amount of infection in secondary diverticulectomies is a factor that may contribute to a prolonged post-operative recovery.

Transurethral resection of the margin of the diverticulum is a dangerous procedure which fails to accomplish the aim of the operation. The margin of safety is small and extravasation of urine is liable to follow.

Within a week or ten days following diverticulectomy transurethral resection or prostatectomy may be performed. If the obstruction is relieved by transurethral resection, the suprapubic catheter may be removed at the same time and the wound allowed to close. If sufficient tissue to relieve the obstruction has been removed, the suprapubic wound heals promptly.

SUMMARY

Diverticulum of the urinary bladder is most often seen in men between the ages of 50 and 70, with benign prostatic hypertrophy. The development of diverticula should probably be ascribed to congenital and acquired factors. The symptoms are not pathognomonic and may even be absent. Complications include infection, calculus formation, tumor, hemorrhage, damage to the corresponding ureter and rupture. The diagnosis may be made from thorough cystoscopic study of the bladder and complete roentgenologic studies of the entire urinary tract. In regard to treatment, the trend is toward conservatism. Retentive diverticula which are badly infected and diverticula associated with stones or neoplasms are indications for removal. Any one of several operative technics may be employed for removal of diverticula depending on the conditions found in the individual case. We prefer performing the diverticulectomy first in cases requiring treatment of obstruction at the vesical neck as well as removal of the diverticulum.

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DISCUSSION.—DR. W. E. LOWER, Cleveland, Ohio: I am very much interested in these two papers because they represent two important urologic problems. They have both been very well presented and treated in a most efficient, conservative way. There are certain factors in diverticulum of the bladder which Doctor Burns brought out and which I think might be repeated for the sake of emphasis.

My own observation leads me to believe that congenital factors do play a rather important rôle in the development of diverticula; otherwise, we should have more diverticula in elderly people who have obstruction, and yet only a small percentage of cases of prostatic hypertrophy have diverticula. The congenital factor was brought out clearly by Dr. Ernest Watson, of Buffalo, in 1923, before the Urological Section of the American Medical Association. He showed by dissection of the fetus in various stages, certain defects that might predispose to diverticula, especially when to this congenital defect was added some obstruction of the bladder outlet. In our own series of cases, which is just under 100, the percentage in women was only 3.9 and in all of these cases there was some obstruction to the urethral outlet, something that prevented easy emptying of the bladder—for example, stricture or caruncle. In cases that require operative intervention to the extent of removing the diverticulum, we have found that by packing the sac with gauze, converting it into a semisolid tumor, the operating for removal of the diverticulum is made much easier.

Doctor Burns has shown that in many of these cases of diverticulum of the bladder associated with obstruction, when the obstruction is relieved the symptoms often subside

and nothing more need be done to the diverticulum. Occasionally a diverticulum will contain a tumor. We have had six such cases and, in that event, of course the diverticulum must be removed. In many cases calculi will be found in the diverticulum and, as a rule, in most of these cases the diverticulum must be removed.

Doctor Burns has well emphasized the question of avoiding cystoscopy in elderly people with prostatic obstruction. It is much better to do it at the time you are prepared to treat the obstruction by transurethral resection and thus avoid the reaction that so often comes from cystoscopy without relief of the obstruction. Whenever we do a cystoscopy, we always give the patient sulfathiazole for about three days following the examination and I believe in this way we avoid many of the reactions that used to follow. Indiscriminate instrumentation in these elderly people often is followed by marked reaction, and I have seen a number of cases in which death followed such instrumentation, especially through the use of metallic instruments.

Doctor Cone brought out the importance of not being in too much of a hurry to bring down these undescended testes. I have seen too many catastrophes occur in an early operative attempt, and I refer principally to the interference with the blood supply, followed by atrophic changes. I think most men who have had experience with this type of case feel that we should wait until puberty, because in many cases the testicle will enlarge at that time and descend into the scrotum, or at least further down toward the scrotum, so that it makes the operation much easier and more promising. I believe we are not conservative enough in many of the lesions of the genito-urinary tract, and until we recognize that certain congenital deformities may not interfere with function, we had better let them alone rather than try to correct them for cosmetic reasons. I refer particularly to certain types of hypospadias. Take the glandular hypospadias; many individuals never know they have it until somebody calls their attention to it when they are adults, and then they are anxious to have something done. I believe a genito-urinary surgeon who has had much experience will agree that, as a rule, you make the condition worse rather than better, and yet the Navy insists that glandular hypospadias must be corrected. It should occur to them that it is not a condition that can be acquired in the service, and certainly does not in any way interfere with function. The same is true of hydrocele in elderly people. The operation on a hydrocele means admitting the patient to the hospital, the loss of two or three weeks' time, and the result often times is just a hard, tender testicle afterwards. At this particular time, when labor is so much in demand, I have found that by aspirating these cases, which can be done under local anesthesia at the office, these men do not lose any time and may not need to have it retapped for from four to six months. I think we might extend this conservatism to even the upper urinary tract and not be in too much of a hurry to do plastics on the hydronephroses until you have pronounced symptoms. Many of these cases must have some type of operation, but I have followed a number in a conservative way by ureteral dilatation, and they have been able to carry on without any great inconvenience.

If all this sounds too conservative, I want to assure you that it comes from my clinical experience over a period of years, and not because I am less keen to operate when I think it necessary; but I believe that it takes years of experience and many failures in too radical a procedure to establish this point of view.

Dr. Malcolm D. Thompson, Louisville, Ky.: I have had no experience with cryptorchidism in children, but my associates and I have performed the Thorek operation upon 20 young adults. In addition, we have examined a number of other patients upon whom the Thorek operation was performed elsewhere. We believe the operation to be justified and of great value—if for no other reason than the tremendous improvement in morale experienced by the patients. As one colored patient surprisingly expressed it, "Doctor, no longer can my friends call me one gone Jones."

It is essential to bring the testicle into the scrotum and onto the thigh without tension. To accomplish this we do not hesitate to divide all the structures entering the testicle, with the exception of the vas and its deferential artery. Doctor Cone said he did not believe the deferential artery sufficient to nourish the testicle in children. As stated, we have had no experience with the operation in children and we do not know whether or not the artery is sufficient in children, but we do know that it is sufficient in young

adults if the testicle is sutured to the thigh without tension. In addition, we have found two procedures to be most helpful. The vas must be gently and patiently mobilized and in some cases as far posteriorly as the seminal vesicle. Also, by dividing the deep epigastric vessels and the other structures of the inguinal floor, the vas deferens can be brought directly out of the pelvis at the external ring, thereby shortening the distance between the seminal vesicle and the scrotum. Even with these aids, occasionally a testicle cannot be brought into the scrotum without tension and we think in these cases, excision of the testicle is advisable, provided there is a normal testicle upon the opposite side.

COL. BRADLEY L. COLE, New York City: I would like to discuss Doctor Cone's paper, and to call attention to its completeness, for it covers most of the controversial points and takes a definite position on them. I would like to subscribe to most of the statements he brought out. Our experience with gonadotrophic stimulation at the Hospital for Ruptured and Crippled* has been unfavorable in those cases in which we felt that descent of the testes had been delayed rather than permanently arrested. There may be some benefit in such cases as those associated with a Froelich syndrome, but hormone therapy in cases of ectopic testes has not been felt to serve any useful purpose, and most of these cases do not present any stigmata that would suggest the need for its use. On the other hand, failure of descent of the testis in a patient with a true Froelich syndrome does not constitute an indication for surgery. A large series of school children were observed by an Australian surgeon for a considerable period of time, and he found, by frequent examination over a period of years, that the majority of those whose testes had not descended when first seen, showed a gradual subsequent descent. He referred to them as instances of "delayed descent." Obviously, operation upon such cases before descent had normally occurred would be unwise. It is partly for this reason that we have felt that operations should be deferred until just before puberty rather than at the age of five or six years, which some earlier authorities preferred, and we have been impressed with the better results obtained in cases where the operation was done at this later period.

I should like to bring out a technical point which is valuable but has seldom been described. In operations for undescended testes, and especially in the ectopic variety, the gubernaculum has an abnormal attachment and does not tend to lead the testis to its proper location in the scrotum. With a retractor held in the lower angle of the inguinal incision, a layer of fascia is seen. It is a natural tendency to assume that the testis should be placed beneath this layer rather than superficially to it. However, if this is done, the testis will never reach its normal location in the scrotum, but will come to lie in an abnormal position in the upper thigh. Instead, one should place it anterior to this fascial layer, between it and the skin, for this layer leads directly to the scrotum.

Incidentally, many of us have seen cases operated upon for hernia where the testis had always occupied a normal position, but following the operation the organ remained high and never regained its scrotal situation. The most frequent cause of this distressing complication is the failure to replace the testis, inadvertently drawn up into the lower angle of the wound during hernia repair, in its normal compartment which has been described previously.

In 1926, Burdick and I reported on the results of 537 cases operated upon by the Bevan method. Satisfactory end-results were seen in only about 50 per cent. It was our belief that the failure of the development of the scrotum was the principal factor in the unsuccessful cases. In 1932, we reported 137 cases in which the Thorek procedure was used, with 123 excellent or satisfactory results, or approximately 90 per cent. The Thorek operation requires that scrotal skin be sutured to the skin of the thigh. Firm union does not appear to take place quite as promptly as is the case in ordinary skin incisions, and there is often a slight tension on the suture line. Therefore, to avoid the embarrassment of having the scrotum separate from the thigh, it is advisable not to remove the stitches too early. This complication is one of the most important in contributing to an unfavorable result.

As regards operating upon cases of undescended testis occurring in soldiers, I am not sure that I agree entirely with Colonel Thompson's and Colonel Higginbotham's

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position.   While I accept the validity of their argument regarding the psychologic reasons for doing this operation, I cannot disregard the fact that three or four months' training is lost in correcting a condition which is congenital in nature, and saving an organ which is without spermatogenic value and whose hormone-producing functions are not essential in view of the normal testis on the opposite side.   Doctor Cone has mentioned the use of a vitalium prosthesis in cases where orchidectomy was required.   It might well be that such a prosthetic substitute would be the answer in some of these cases.

DR. EDGAR BURNS, New Orleans, La. (closing): The first large diverticulum was operated upon by Doctor Lower's technic; it facilitated removal a great deal.

DR. ROBERT E. CONE, Galveston, Texas (closing): I have little to add, but should like to show one lantern slide.   Here you see our results after the Thorek operation. You will note we can depend on a low scrotal position following this procedure.   In the 20 per cent in which structure was subnormal the blood supply of the testicle may have been injured in a few during the process of cord lengthening.   In the remainder testicular development was anomalous or normal growth was deficient.   Postoperative hormonal stimulation has been of no benefit in this group.

THYROID CARCINOMA WITH METASTASES: STUDIED WITH RADIOACTIVE IODINE*

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IN 1942, in a preliminary note in Science we reported our first case of storage of radioactive iodine in a metastasis from a thyroid carcinoma. The patient was still under observation. We present now the completed report of this one case which was followed until death, and in which the autopsy findings are of considerable interest. Our original statement about the time of removal of the primary growth must be corrected. The patient had deliberately falsified her history, and it was only after her death that, through her relatives, we were able to ascertain the facts.

CASE REPORT

M. R., P.H. No. 652642: Negro, female, age 39, single, houseworker, was admitted to St. Luke's Hospital, New York City (St. L.'s Hosp. No. 259205), June 27, 1934, complaining of a swelling of the neck of seven years duration. The mass had been the "size of a quarter" for the first five years, but in the two years prior to admission it had grown to the "size of a lemon," and gave her a sensation of pressure and obstruction to breathing on exercise. Through the courtesy of Dr. Leila Charlton Knox, Pathologist, we learn that an encapsulated, extremely vascular tumor was removed June 28, 1934, from the isthmus of the gland (S.P. No. 47764). This measured 7 x 6 x 5 cm. and had the appearance of an adenoma of the fetal type (Fig. 1). There was never any local recurrence demonstrable clinically.

On September 2, 1941, seven years after operation and 14 years after the tumor was first noticed, the patient sustained a pathologic fracture of the left humerus. This occurred with a minimum of trauma. She had been supporting a considerable part of her weight on her left arm while filling a clothes hamper when she experienced sudden severe pain high up in the left arm, accompanied by an audible crack. She was admitted to the fracture ward of the Presbyterian Hospital where physical examination showed no palpable deformity. There was marked limitation in abduction because of pain. A roentgenogram (Fig. 2) showed areas of bone destruction in the shaft of the humerus near the deltoid tubercle, and a small fracture line on the medial border. The patient then acknowledged having had transient pains in this region for several months. The rest of her history, as given then, was irrelevant. She denied any illnesses or any operations.

On general physical examination, there were only two significant findings: The first was a soft, pulsating oval tumor mass about 8 cm. in diameter projecting 4 cm. above the scalp in the region of the left parietal bone (Fig. 3). This the patient considered a wen, and said it had been growing for about seven years, without pain. There is no record of its presence, however, in her chart at St. Luke's Hospital. The second finding of interest was a low collar scar present in the anterior neck. The thyroid gland was barely palpable and not nodular. The patient denied knowledge of the scar but, finally,

after intensive questioning, found a friend who "remembered" that an operation for tumor had been performed when the patient was five years old!

Further roentgenograms showed areas of bone destruction in the lower end of the right femur (Fig. 4), the upper end of the left femur (Fig. 5), and in the left parietal bone (Fig. 6) underneath the "wen," where there was a defect involving the inner as well as the outer table. Films of the chest showed some increases in the lung markings throughout, with rather prominent peribronchial fibrosis at both first and second interspaces on the left, interpreted as fibroid tuberculosis. This had been noted at St. Luke's Hospital seven years earlier. The patient's sputum was never positive, and
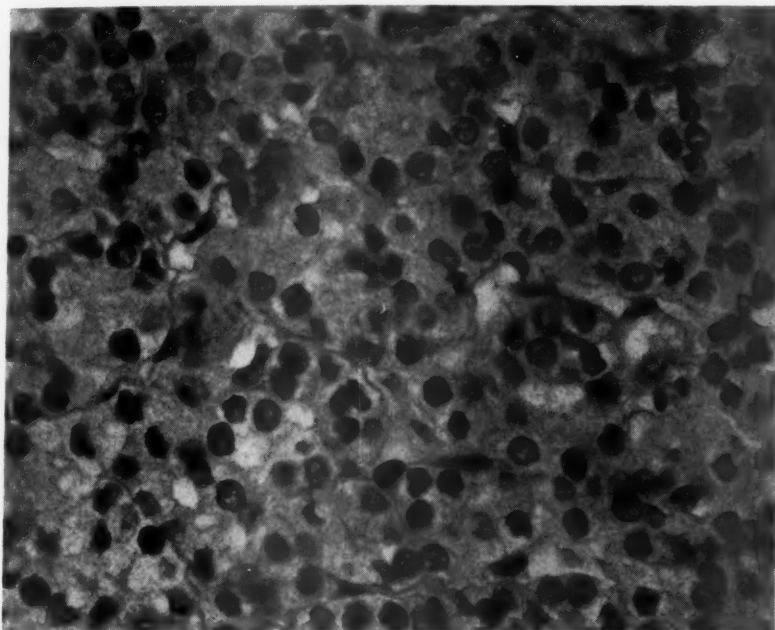

FIG. 1.—St. Luke's Hosp. No. 47764. Photomicrograph (×875) of encapsulated tumor removed June 28, 1934. Courtesy of Dr. Francis Carter Wood. The photograph shows a tumor with the appearance of a well differentiated adenoma.

her only suggestive history was a single attack of "pleurisy" many years before. Serum calcium, phosphorus, and phosphatase were within normal limits. There was no Bence-Jones protein in the urine.

The left arm was placed in a swathe bandage and sling and radiotherapy was begun. A needle biopsy of the tumor in the left parietal region yielded a small blood clot, 2 mm. in greatest diameter. On microscopic examination (Fig. 7), an adenomatous tumor was recognized, with a few small colloid follicles. It was thought at the time impossible to obtain any further information about the original tumor. Subsequently, however, it could be compared with the sections made at St. Luke's Hospital, as shown in Figure 1. When the nature of the tumor was recognized, basal metabolic rate and serum cholesterol determinations were made. These were within normal limits and remained so throughout her course.

Considerable progress had been made with radiotherapy before a first tracer dose of radioactive iodine was given. In the first seven weeks 3400 r. was given through four portals to the lesion in the humerus, using 200 K. V., 1 Mm. copper, and 1 Mm. aluminum filtration at 50 cm. anode-skin distance. Two weeks after treatment had begun and about 1200 r. had been given, the pain had almost completely subsided, and at the

end of the treatment the patient was free from pain although abduction of the left arm was limited to about 70°. The patient continued to work during the treatment. About three weeks after irradiation was given to the left arm and eight weeks following the fracture, the patient complained of pain in the right lower thigh. A dosage of radiotherapy (1200 r.) was given this area through one anterior and one posterior portal, using the factors noted above. The patient also complained of throbbing in the scalp tumor, and this showed an increased amplitude of its pulsations. Accordingly, 600 r. was given through one portal, using the same factors as above. A dosage of 600 r. was given the left upper thigh through one portal. For reasons which are not certain, the pulsations

Fig. 2.—Roentgenogram of the left humerus, April 19, 1942, showing bone destruction. This had been the site of the pathologic fracture.

in the tumor of the parietal bone decreased markedly after 600 r., and the tumor became much softer.

Treatment to these two fields was then interrupted for the administration of a tracer dose of radioactive iodine (eight-day half-life). This was obtained through the courtesy of Prof. E. O. Lawrence, of the University of California. It was given orally in water on December 5, 1941. The substance was taken up, as shown by the Geiger counter, in considerable quantity by the metastasis in the right femur, and by the

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FIG. 3.—Photograph of patient, February 7, 1942, showing epilation over tumor in the left parietal region following treatment 600 r. Subsequently there was a regrowth of hair in this region.

FIG. 4.—Roentgenogram, January 16, 1942, showing bone destruction in the lower extremity of the shaft of the right femur.

FIG. 5.—Roentgenogram, April 19, 1942, showing bone destruction in the proximal portion of the shaft of the left femur and lower margin of the left ilium just above the acetabulum.

FIG. 6.—Roentgenogram of skull, April 19, 1942, showing an area of bone destruction in left parietal region.

thyroid gland. It was not stored in any appreciable quantity in the other bony metastases. As the parietal bone lesion was soft, almost fluctuant, it was considered possible that spontaneous, or radiotherapy-induced necrosis, might account for lack of storage in these foci. After this, as well as after other tracer doses, the rate of disappearance of radioactive iodine from the right femoral metastasis paralleled closely that of the thyroid gland. The radioactive iodine in both the thyroid gland and in the right femoral metastasis could not be "washed out" by the administration of 54 mg. of potassium iodide, which indicates that the iodine was bound in these foci, probably in organic combination.

Because of the localization in one metastasis, however, it was suggested that a larger dose might afford selective therapeutic "internal irradiation," and ten millicuries was
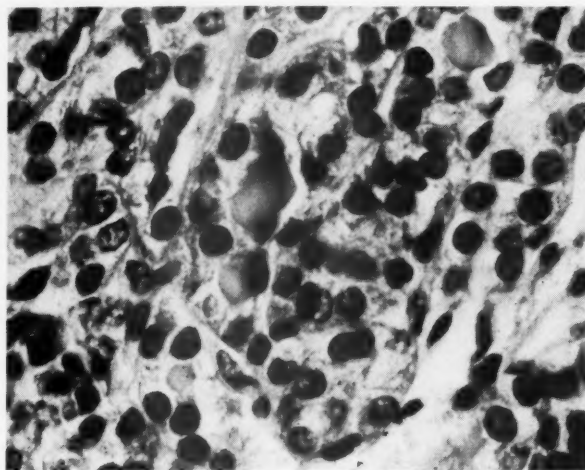

FIG. 7.—S. P. No. 79954: Photomicrograph of the tumor showing four small colloid follicles, all that were found in the tiny needle biopsy from the skull metastasis.

accordingly given, mainly of the 12.6-hour period, obtained through the courtesy of Prof. Robley D. Evans, of the Massachusetts Institute of Technology. Again there was localization, about 6 per cent of the material in the thyroid and about 30 per cent in the right femoral metastasis. Radio-autographs of the latter were made by placing a film on the patient's thigh. The area on the film darkened by the radiation tallied with the localization obtained by the Geiger counter and by roentgenograms.

The right femoral metastasis showed no change in radioactive iodine content during the first week, but when measured again at the end of three weeks showed loss of 85 per cent of its radioactive iodine. A tracer dose given a few days later showed no further uptake by the metastasis although there was new localization in the thyroid. This was interpreted at the time as evidence of the effectiveness of this "internal irradiation." At least the iodine fixing function of the metastasis had been impaired, and it was hoped that the growth and multiplication of the tumor cells might also have been inhibited.

Blood and urine samples were taken at intervals after administration of the therapeutic dose, and the amount of radioactivity determined (Charts 1 and 2). These curves might be of interest in other cases where radioactive iodine might be used in calculation of the amount of radiation delivered in the body before localization of the radioactive iodine. Since there is an appreciable period where large amounts of radioactivity are in the body before localization, it should be possible to deliver proportionally more radiation to

regions where localization occurs, by using the eight-day period of iodine rather than the 12.6-hour period. However, the radiation is here administered slowly and would not be as effective as the same number of roentgens delivered by the shorter-lived isotopes.

The patient remained in apparent good health until July, 1942. Repeated roentgenologic examinations failed to show any appreciable change in the areas of bone destruction. In July, 1942, she awoke one morning with a feeling of numbness and tingling in the legs. Roentgenograms made at this time were interpreted as showing no new lesions.

% TOTAL DOSE OF RADIO-IODINE PER LITER OF BLOOD

10 millicuries given orally
containing <0.5 mg Iodide Ion

HOURS AFTER DOSE
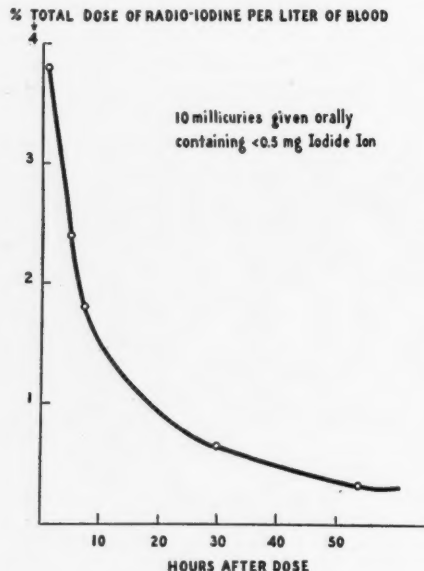
CHART 1.—Curve showing percentage of total dose of radio-iodine per liter of blood.

% OF TOTAL DOSE EXCRETED IN URINE

HOURS AFTER DOSE GIVEN
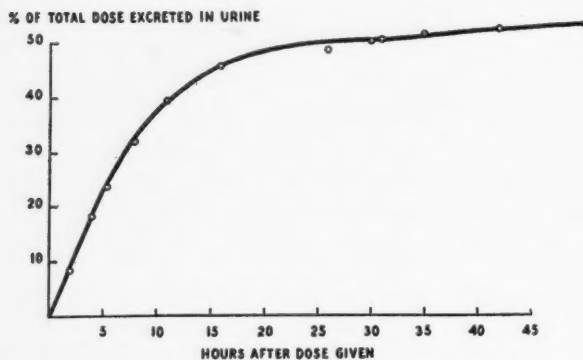
CHART 2.—Curve showing percentage of total dose of radio-iodine excreted in the urine.

The patient became discouraged and failed to keep clinic appointments, in spite of social service follow-up, from August 11 until October 26, when she was admitted to the hospital with loss of power in both legs. She said this had come on suddenly two weeks before admission, and that she had had pain in the back. Neurologic examination, by Dr. E. G. Zabriskie, showed a sensory level extending from the ninth thoracic down, in which pain and temperature were both involved, excepting the sacral areas. Touch was moderately diminished at the same level, but included the sacral areas. Vibration

was lost from the ninth segment downwards. There was profound disturbance of gross muscle power in both legs, the left more so than the right. There was a curious mixture of flaccidity and spasticity in both legs, with bilateral patellar and ankle clonus, and bilateral Babinski.

Roentgenologic examination (Fig. 8) was reported as follows: "Films of the skeleton show a destruction of the pedicles of the 9th and 10th thoracic bodies on the left side, along the border of which there is a soft tissue mass, due to tumor which has invaded
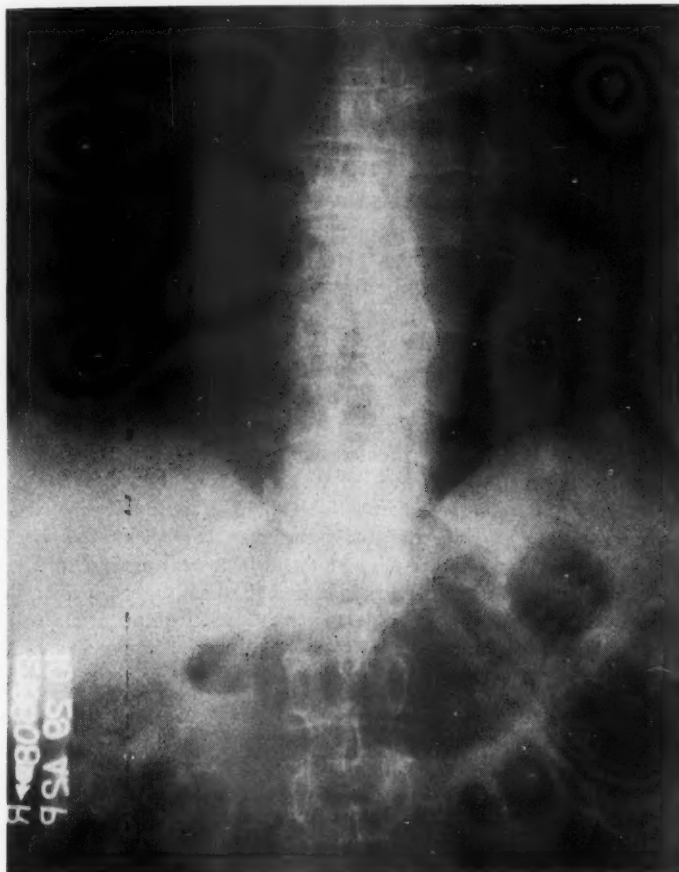
Fig. 8.—Roentgenogram, October 26, 1942, of the spine, showing destruction of the pedicles of the 9th and 10th thoracic bodies on the left, with a soft tissue mass.

underneath the ligamentous investment of the spine. Apparently there is intraspinal tumor here which has grown out through the intervertebral foramen and then invaded on the outside of the spine as well. The body of the vertebrae itself is not badly involved."

Further careful review of all films, by Dr. Ross Golden, after the patient's death led to the finding of changes in these pedicles in the first skeletal films, taken at the time of the first hospital admission on September 9, 1941. The changes are slight, however.

Because of the definite clinical and roentgenologic findings of spinal metastases, a tracer dose of radio-iodine, obtained through the courtesy of John R. Dunning, of Columbia University, was given in November, 1942. This again showed uptake of

radioactive iodine by the thyroid and right femoral metastasis and did not suggest appreciable uptake in other regions. The femoral metastasis here took up about three times more iodine than the thyroid gland.

It must be kept in mind that a count obtained over a region with the Geiger counter depends on the gross composition of the tissues underneath it as well as on the amount of radioactive material present. The inverse square law of radiation is also a factor in the count, so that proximity to the radioactive source is of great importance. These factors make difficult the interpretation of counts not far removed from background, especially in regions near foci containing large amounts of radioactivity, or over regions like the abdomen where moderate counts are obtained for several days because of some residual unabsorbed iodine, possibly in the organs, possibly in the large amount of blood subtended by the counter. This is especially true for the period of the first few days following dosage. The interpretation of the count over the small of the back was uncertain, because the counter subtended the abdomen and moderate counts of the same order were also obtained over the abdomen. While it was impossible with the amount of radioactive iodine made available in November, 1942, to exclude a spinal metastasis, it was not possible to state that the counts suggested any appreciable amount of iodine-containing tissue in the spine. Certainly nothing approaching the uptake of the right femoral metastasis or of the thyroid could be demonstrated in the vertebrae.

Palliative radiation was given to the lower thoracic spine, with striking relief of pain but no marked change in the paralysis. The patient was bedridden, but, when relieved of pain, in excellent spirits, optimistic, and in good general health. Further palliative radiation by roentgen ray was necessary for the spine in January, 1943, and for progression of tumor, now obviously invading soft parts, in the right humeral metastasis, in April and June, and the left upper femoral metastasis in May. Some relief was always obtained.

Various forms of physiotherapy were exhibited. The most effective, at least psychologically, was massage. In spite of steady increase in the size of her lesions her nutrition was maintained, and she required only codeine and aspirin for sedation. The patient had great faith in the radioactive iodine, and thought that further dosage might relieve her paralysis. It was not possible to obtain sufficient material for therapy, but two more tracer doses were administered as psychotherapy, in April and May. These again showed uptake of radioactive iodine by the thyroid and the right femoral metastasis. No other foci were demonstrable with certainty by the Geiger counter. The right femoral metastasis took up six times more than did the thyroid gland, which was about as much as it took up before the therapeutic dose of radioactive iodine.

It may be of significance that the right femoral metastasis which took up five times as much iodine as the thyroid gland before treatment with the therapeutic dose, took up no radioactive iodine three weeks after the dose was given, and had lost most of its radio-iodine. As time went by the uptake became larger (Chart 3) until the last tracer dose it took up, again, six times as much as thyroid. This would suggest a temporary impairment of the iodine storage function with a gradual restoration of function, very probably due to increase in size of tumor.

In May, after six months of bed care, the first indications of a downhill course were evident. The tumors grew more rapidly. Pain increased, and the patient began to run a fever. In June there was increasing edema of the whole left lower extremity; fever was higher and the patient had frequent, profuse diaphoresis. Morphine was not necessary, however, until eight days before death. Cough was not a symptom, but the patient had been taking fairly regular doses of codeine. The first roentgenogram to show striking lung lesions was taken July 1, after a sudden change for the worse, initiated by a shaking chill. On review of previous films, even with the knowledge of the distribution of lesions at autopsy, Dr. Ross Golden felt that no definite diagnosis of lung metastases could be made before this date.

Following the chill the patient rapidly became weaker. Her white blood count, which had been followed throughout her course because of the radiation therapy, rose, reaching 21,600, with 87 per cent polymorphonuclear leukocytes. Labored respirations were first noted on July 11, irregular fever and rapid pulse continued, and she died on July 20, 1943, 16 years after she first noted the tumor, and nine years after its local removal. Because of the unreliability of the history it is not possible to say how long she had clinical evidence of metastases before death, but five years seems a conservative figure.
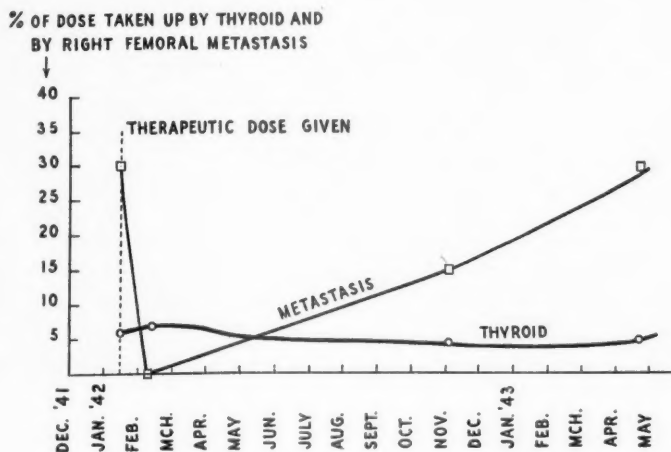

CHART 3.—Curves showing percentage of total dose of radio-iodine taken up by the thyroid and by the right femoral metastasis.

It had been our intention, if therapy failed, when the patient was obviously *in extremis*, to administer a final dose of radio-iodine so that, if permission for autopsy were granted, we might be able to make a quantitative analysis of the uptake and demonstrate by radio-autographs the material in the tissues as it might be selectively absorbed. The patient's death, in spite of her long course and obviously terminal stage, was unexpectedly sudden at the end, and the radio-iodine was not administered.

Autopsy.—This was performed 28 hours after death by Dr. Clarence Schubert, of the Department of Pathology, with a final anatomical diagnosis as follows:

CARCINOMA OF THYROID

Obsolete operation: Thyroidectomy

Secondary carcinoma in thyroid with extension to parathyroid, heart, lungs, pleura, diaphragm, liver, adrenals, kidneys, and bones (parietal—left, with extension to dura; humerus—left, femora and vertebrae—T 9–L 2 inclusive, with extension to extradural tissue of thoracic cord)

Myelomalacia—T 10–T 12

Edema of lung

Acute serofibrinous pleurisy, with hemorrhage

Fatty liver

Medial degeneration of aorta

Myomata of uterus

Polypus of uterus

Polypi of colon

Melanosis of colon

Foreign body in peritoneal cavity—detached appendix epiploica

677

FIG. 9.—Autopsy No. 14184. Photograph showing 1.2 cm. tumor nodule in the lower pole of the left lobe of the thyroid.

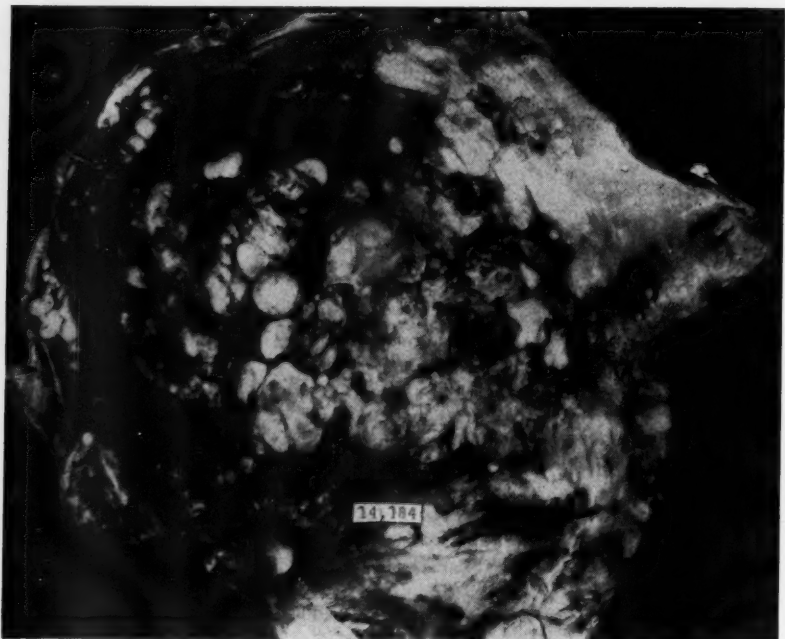FIG. 10.—Autopsy No. 14184. Photograph of lung showing multiple metastatic nodules.

FIG. 11.—Autopsy No. 14184. Photograph of diaphragm showing multiple metastatic nodules in pleura.

The significant gross findings externally were the excellent state of nutrition and the absence of any decubitus, the mass in the left parietal region, the swollen left upper arm, with discoloration and peeling of the skin following irradiation, and the edema of the lower extremities.

On section, there were certain striking features. There was a tumor in the thyroid gland, which was found, with no other gross lesions in the gland, as a 1.2-cm. nodule in the left lower lobe (Fig. 9). It was circumscribed, but not encapsulated, firm and pale yellow-

FIG. 12.—Autopsy No. 14184. Photomicrograph
of left parietal bone showing metastatic nodule.

gray. There were multiple metastases in the lungs (Fig. 10) and pleura (Fig. 11). *No lymph nodes were involved.* The osseous metastases corresponded in their distribution with that shown in the skeletal films. A portion of the parietal bone was removed for study (Fig. 12), and showed the tumor adherent to the dura but not extending to the brain. The tumor tissue from the other bones, with the exception of that in the vertebrae, was obtained through small exploratory incisions, and the gross involvement was not seen.

The other metastatic lesions were less dramatic. The interesting feature of the metastases, however, was the absence of any gross resemblance to thyroid tissue, except in the tumor removed by curette from the lower end of the right femur, which had consistently shown iodine uptake during life. This was soft, pale, red-brown tissue, with the color and consistency of thyroid. The other lesions, pulmonary, pleural and osseous, which had shown no iodine uptake, were soft, mottled yellow and gray, often necrotic, but not suggestive of thyroid.

FIG. 13
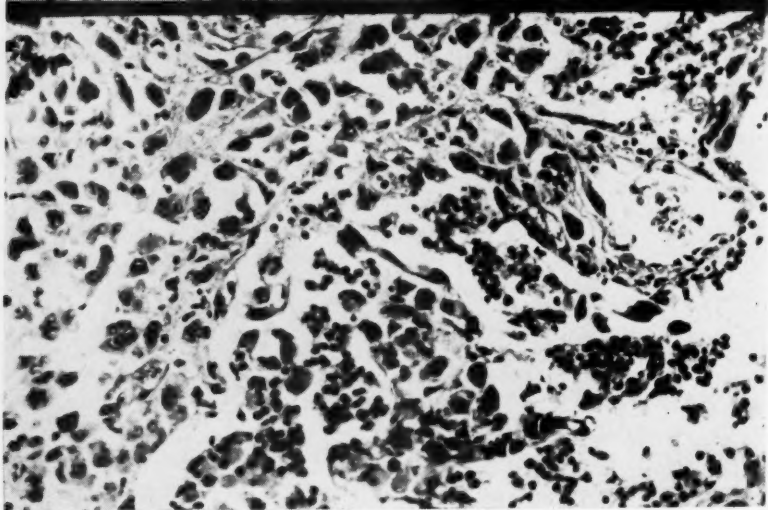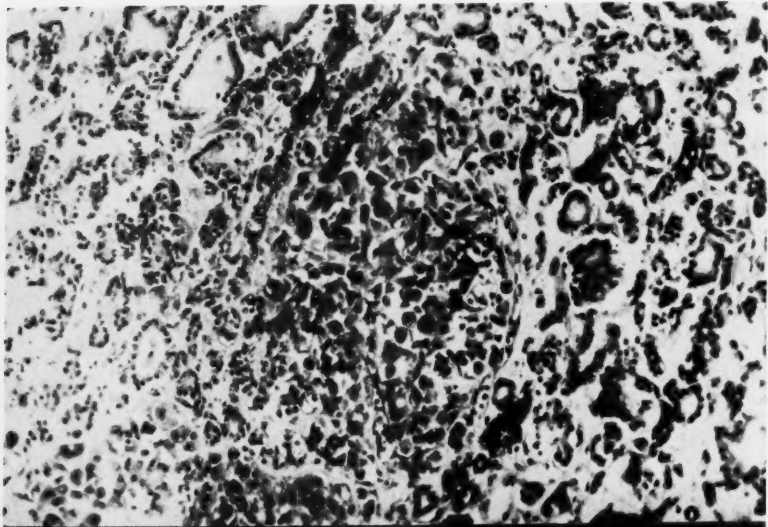
FIG. 14

FIG. 13.—Autopsy No. 14184. Photomicrograph of tumor from right femur, a field showing some undifferentiated tumor. A great bulk of this metastasis, however, was well differentiated.

FIG. 14.—Autopsy No. 14184. Photomicrograph of tumor in thyroid showing undifferentiated carcinoma without colloid follicles.

Fig. 15
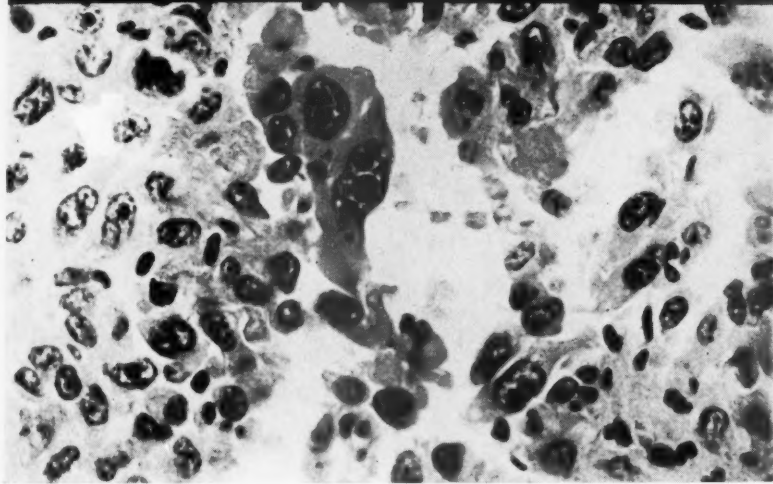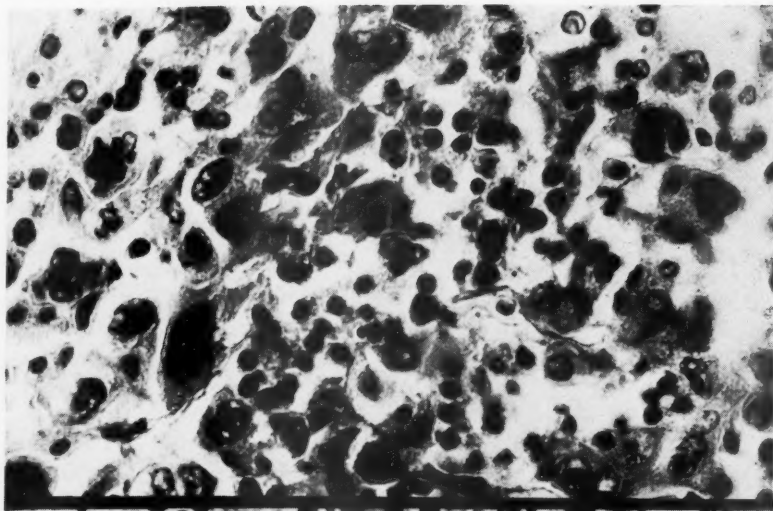
Fig. 16

Fig. 15.—Autopsy No. 14184. Photomicrograph of tumor from lung showing anaplasia and multinucleated cells.

Fig. 16.—Autopsy No. 14184. Photomicrograph of tumor from heart showing bizarre gigantic cells.

FIG. 17

FIG. 18

FIG. 17.—Autopsy No. 14184. Photomicrograph of tumor from the liver showing spindle cell metaplasia.

FIG. 18.—Autopsy No. 14184. Photomicrograph of tumor in the 11th thoracic vertebra; an illustration of the highly differentiated form with colloid follicles.

Microscopic Examination: The microscopic study of the different lesions confirmed the impression received from the gross examination, that this was a most unusual type of thyroid tumor. Most of the tissue from the right femur (Fig. 13) was well differentiated, made up of small acini lined by flattened epithelium. These varied somewhat in size, but were all smaller than the average size of normal thyroid acini. Some contained colloid, and others a faintly eosinophilic granular precipitate. In a few small areas, however, there was undifferentiated tumor.
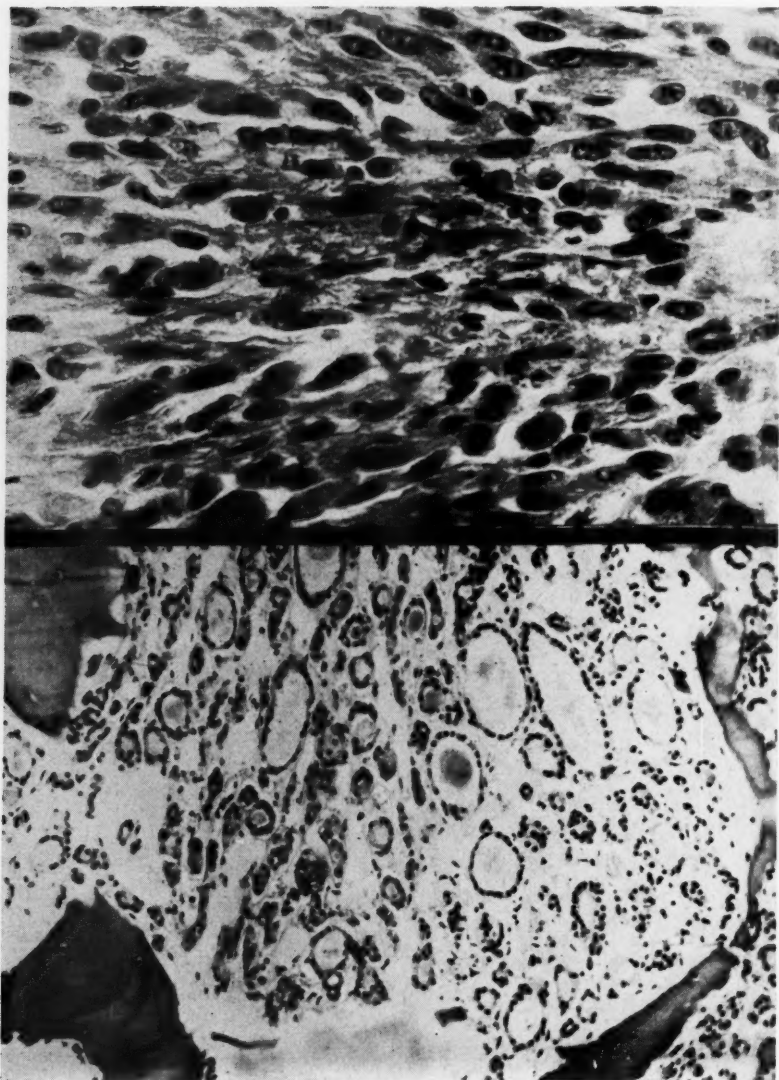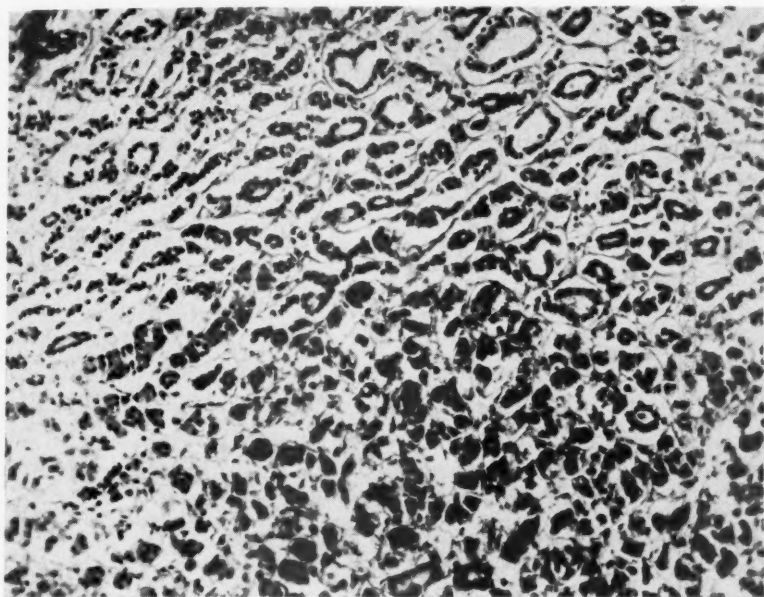

Fig. 19.—Autopsy No. 14184. Photomicrograph of tumor from left femur; a field showing varying degrees of differentiation.

This undifferentiated tumor, which was found to compose the bulk of all the other lesions studied, including the nodule in the left lobe of the thyroid gland (Fig. 14), bore no resemblance to normal thyroid or thyroid adenoma. It was composed of cells which varied widely in size, shape, and staining characteristics (Figs. 15, 16 and 17). For the most part they were large, irregular, often elongated polyhedral structures, with eosinophilic cytoplasm and very large irregular nuclei, often containing large quantities of chromatin. Multinucleated forms, often gigantic, with large nuclei, were common. In almost all of the cells not in mitosis there were within the nuclei large globular eosinophilic masses surrounded by a clear zone. Most commonly there was only a single one of these inclusions, but as many as five were occasionally seen within a single nucleus. In most high power fields there were three to five mitotic figures, but, in addition, there were nuclei which appeared lobulated, or partially divided, as well as the binucleated and multinucleated forms. The mitotic figures were very irregular and frequently multipolar.

Differentiated tumor, however, was found, as has been said, in the bulk of tissue from the right femur, and also, in less amount, in the parietal bone and the 11th thoracic vertebra (Fig. 18). No significant uptake of iodine had been demonstrated in the latter two sites. From the gross appearance of these lesions it seems probable that the bulk of the tissue was undifferentiated. In some fields there was at one extreme rather typical thyroid-like tissue, with colloid secretion, and in others, the wildly anaplastic

tissue described. Intermediate between these two types there was occasionally a solid adenomatous, or sometimes tubular arrangement, closely resembling the original tumor. These three types of tissue might be found in the same metastatic nodule, notably in the left femur (Fig. 19), but they were usually distinguishable even if there was intimate intermingling of the cell types.

DISCUSSION.—It is of some interest to review briefly the historical background which led to this clinical investigation. It should be emphasized that carcinoma of the thyroid varies in its clinical course, and that this, to a certain extent, can be correlated with the histologic appearance of the tumor. The highly malignant anaplastic carcinomas which have no organoid arrangement, produce no colloid, and grow with extreme rapidity, often causing death by local disease alone, cannot be expected to function as thyroid. A small group of tumors midway between the completely undifferentiated and the highly differentiated forms do not suggest, from their morphology, that much endocrine activity might be expected. But the more benign forms do suggest functional tissue. These, often grouped under the misleading heading of "adenoma malignum," the very term being a contradiction, fall into two main groups, and constitute, in our experience, the great majority of thyroid cancers. These two groups are for the most part clear-cut clinically and pathologically. There is the papillary form, often colloid-containing, which is exceedingly common when the tumor involves lateral aberrant thyroid tissue, and which metastasizes usually to lymph nodes and later to the lungs. This type rarely involves bone. There is the type which resembles embryonal, fetal, or simple adenoma, and is often so well differentiated as not to suggest neoplasm histologically, even in the metastatic deposits. This type may be enucleated and without local recurrence be found, often several years later, widely disseminated in the bones.

Historically, recognition in this form dates back to Müller (1871), who noted, with interest, the similarity to the normal organ in the primary tumor as well as in the metastases. Eberth (1872) reported such a case in a dog. Runge (1876) failed to recognize the import of a vertebral tumor containing colloid follicles. That same year Cohnheim wrote the now famous article on "Simple Colloid Goiter with Metastases."

The question of the possibility of function in these tumors was raised by Gulliver, in 1886, when he reported a case of myxedema in which the symptoms were not relieved by the development of a thyroid carcinoma with metastases. But the proof of the potential function came shortly afterwards, in 1894, and has never, to date, been so dramatically repeated. von Eiselsberg reported a woman who, after total thyroidectomy by Billroth, in 1886, developed myxedema and tetany, which disappeared three years later with the growth of a metastasis in the sternum, so proved by operation.

The next step in the study of the metastases of these well differentiated tumors in which colloid had been apparent grossly and microscopically, and to which the terms "benign metastasizing goiter," "wuchernde struma," and "adenoma malignum," had been given, was chemical analysis for iodine

content. Iodine has been demonstrated in such metastatic deposits by Ewald (1896), Gierke (1902), Steim (1904), and Meyer-Hürliman and Oswald (1913). Other investigators failed to demonstrate iodine (Regensburger, Marine, Zapelloni, Wegelin and Abelin, Eisen. Excellent summaries of these tumors are by Branovacky-Pelech (1926), and Simpson (1926). In addition, Simpson's article abstracts the cases to date and adduces strong evidence that all these osseous metastases, however much they resemble normal thyroid, or benign thyroid adenomas, are carcinomas with a primary growth in the thyroid.

Another approach to the study of function in these tumors is the analysis for active hormone. This was first attempted in animal experiments by Meyer-Hürliman and Oswald, in 1913, in material obtained from fluid in a sternal metastasis. Twenty years later, Engelstad (1933) obtained active thyroid colloid from a metastasis in the cranial vault, tested in mice as protection against acetonitrile, and repeated this on a bone metastasis in another case reported three years later. A year later, Milles (1934) obtained from a case with lung and bone metastases an extract from the lung metastasis which accelerated growth and maturation in tadpoles. Similar biologic proofs with mice and tadpoles were given by Dickson, Diveley and Helwig (1940). They presented a case with a massive recurrence in which they considered that thyrotoxicosis had developed. This is not substantiated by their given clinical data, and no autopsy was obtained, so that the thyroid gland itself was not investigated. It is of some interest that similar studies have been made on thyroid tissue appearing, not as metastases, but as an independent tumor in the ovary, "struma ovarii colloides," and that there is considerable evidence that this tissue also can function as thyroid.

When the radioactive isotope of iodine became available, it afforded a comparatively easy method of checking upon the physiologic function of iodine storage in metastases from thyroid carcinoma. The employment of radioactive iodine in the study of thyroid physiology has been carried out largely in two laboratories, the University of California, where Lawrence developed the cyclotron, and Evans, at the Massachusetts Institute of Technology in collaboration with Means of the Massachusetts General Hospital. The radioactive iodine produced by the cyclotron is mixed with inert iodine compounds such as potassium iodide, and usually administered, by mouth, although in certain experiments the intravenous route has been used. The proportion of radioactive to inert elements is one to 10^{10} or 10^{15}. The radioactive element behaves physiologically and chemically in every way the same as the inert, so that the radioactive element follows the course of the inert element in the body. The radioactivity in the tracer dose is kept so small that no effect on the organism due to its radioactivity occurs. The property of *gamma*-ray radioactive iodine makes it possible to follow its course in the intact animal by means of the Geiger counter.

In the early investigations with radioactive iodine the rate of absorption from the digestive tract was compared with four other radioactive ele-

ments: sodium, potassium, chlorine, and bromine. When the radioactive elements were administered by mouth in isotonic solutions their appearance in the hand was noted within three to six minutes. There was little difference in absorption rates between the elements except potassium which was absorbed more slowly; after an hour only 48 per cent, while all others, 75 per cent to 85 per cent, had been absorbed.

Following these studies comes the observation that the thyroid gland takes up iodine selectively up to the point of saturation, as might be expected from earlier chemical analyses of thyroid glands for iodine. Hyperplastic and hyperthyroid glands take up more iodine than normal glands. Also it was observed that excessive amounts of inert iodine administered with the radioactive element reduced the amount of the latter which was fixed by the gland. This has a bearing on the use of iodine clinically. The average normal gland contains between 20 and 25 mg. of iodine. Hyperplastic glands may have a much greater capacity for fixing iodine. After saturation further administration of iodine serves no useful purpose although there is certain daily turnover, greater in toxic than normal glands. To maintain saturation, therefore, a small daily amount of iodine is necessary. Indeed it has been shown that as good clinical effects can be produced by the daily administration of one drop of Lugol's solution containing 8 mg. of iodine as by giving one cubic centimeter containing 120 mg.

Through the use of the radioactive element it has been shown that the thyroid gland of all types takes up iodine with great rapidity, i.e., within the first few hours after administration. However, a marked variation from normal occurs in the toxic goiter where, in from one to four hours, the maximum is reached and immediately the iodine is discharged until a saturated level is reached. The hyperplastic nontoxic gland falls in between the normal and toxic in that it reaches the maximum within the first 24 hours and holds it. The atrophied gland of myxedema takes up small amounts of iodine, and takes it up slowly. Hamilton, Soley, and Eichorn reported two cases of carcinoma of the thyroid studied by giving radioactive iodine before operation. The malignant tissue removed showed only one one-hundredth the amount of the tracer iodine found in the normal tissue taken at the same time. From the appearance of their photomicrographs, however, it seemed to us that they were not dealing with well differentiated types.

These observations lend support to previous ideas concerning iodine function. The normal glands are in a state of iodine equilibrium, although having the capacity to store a certain excess, if available. The hyperplastic gland is hyperplastic, according to the most widely accepted hypothesis, because of iodine insufficiency, hence its great avidity. With toxic glands the normal storage and release of the iodine containing hormone is lost. The gland is depleted of iodine, takes it up with great speed and in relatively large amounts, but is unable to hold all it takes up. This property of the toxic gland, as it concerns radioactive iodine, may possibly be useful in diagnosis in borderline situations. The reduced capacity of the atrophied

gland to take up iodine is what might be expected. As for the carcinomatous tissue, chemical analyses reveal low iodine content except in the adenoma malignum type.

In our own clinical investigation tracer doses of radio-iodine have been given to several cases besides the one reported in detail above. In two cases of colloid-containing bony metastases there was no uptake. One of these was a so-called Hürthle cell tumor, which might be functionless, but the other was a well differentiated adenoma malignum type. The lack of uptake in this latter case was a surprise, and the significance of the finding is not clear.

One case of a child with total thyroidectomy and possible metastatic tumor not demonstrable roentgenologically is being studied. The site of persisting disease has presumably been located by the Geiger counter and radioautographs. Further confirmation is needed, and this case will be reported later. In approximately 150 carcinomas of the thyroid in the Presbyterian Hospital we have no instance in which hyperthyroidism could be attributed to the tumor tissue. If such a case were ever found, the study might be most illuminating.

SUMMARY

A case has been reported, thought to be the first in which the function of metastases from thyroid carcinoma has been studied by means of radio-iodine storage.

Only one metastasis consistently showed appreciable uptake of the material.

At autopsy, the bulk of the metastatic tissue was undifferentiated. The metastasis which showed consistent uptake of iodine was the only one which grossly resembled thyroid tissue, and which, microscopically, showed chiefly well differentiated tumor.

No other case has come to the authors' attention in which thyroid carcinoma of the adenoma malignum type has shown anaplastic changes. The autopsy findings were a great surprise and are, we believe, extremely unusual. The histologic character of the undifferentiated type of tumor was such that an earlier fatal outcome might have been expected on the basis of previous experience with tumors of this morphology.

There was no clinical evidence that the radio-activity of the iodine was effective, in the amount given, in therapeutic "internal irradiation." It is possible that larger amounts might be effective in a lesion in which only well differentiated tumor was present.

We know of no evidence that external irradiation, by radium or radiotherapy, of thyroid carcinoma may change the histologic character of the tumor. We believe that two types of tumor were present in this patient before the administration of the radio-iodine as, from the outset, there was no uptake in most of the lesions with tracer doses.

CONCLUSIONS

Since some well differentiated tumors of the thyroid are capable of storing iodine, it is thought that in selected cases, possibly where the amount

of tumor tissue is small, effective therapeutic internal irradiation of metastases may be achieved with large enough doses of radioactive iodine. There should be minimal damage to other tissues because of the selective absorption.

Tracer doses of iodine may be valuable diagnostically, but only if there is localization. Failure of uptake does not mean that the tumor in question is not of thyroid origin.

Further study of thyroid carcinoma by this method is indicated.

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MODIFIED TECHNIC IN SKIN GRAFTING
OF EXTENSIVE DEEP BURNS

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Many reports in the recent literature have emphasized the fact that all patients with extensive deep burns develop serious malnutrition as a result of the presence of a very large open wound.[1, 2, 3] This occurs despite forced nutrition, frequent transfusion of whole blood and the earliest possible skin grafting. At this clinic we have had an opportunity to treat a moderate number of patients with deep burns of 30 per cent, or more, of the body surface. The large majority of them have survived the stages of shock and burn toxemia; a few have died during the necessarily long stage of healing. Thus any technic of skin grafting, which will speed the healing of a large burn wound may save lives. We have developed two modified technics which have been useful. Inasmuch, as neither of them has been stressed in recent books and articles on skin grafting, we have felt it worth while to report our experience.

EARLY SURGICAL DÉBRIDEMENT WITH IMMEDIATE SPLIT-THICKNESS GRAFTING

Deeply burned areas, whether primarily treated by ointment or tanning methods, are ordinarily not free of slough and ready for grafting until the fifth week. By the tenth day, however, the patient has usually passed through the phases of shock and toxemia, and is at that time in better nutritional condition than he will be at any other time during the phase of healing. The body reserves of protein are not yet fully depleted and adequate serum protein levels can be maintained with the aid of high protein feedings. Severe anemia may be prevented by blood transfusion. Extensive surface infection of the burned area has not usually occurred because the wound is still sealed off by the densely adherent necrotic skin. This would seem to be the logical time to start skin grafting, and experience has shown that grafting can be successfully accomplished immediately following a clean, sharp surgical débridement. The débridement must be carried down to normal unburned tissue whether it be fat, fascia, or muscle. By the tenth day it is always possible to recognize dead from living tissue. Hemostasis is not difficult to achieve.

Split-thickness skin grafts can then be applied to the freshly débrided areas and, in our experience, they take as well on these areas as they do on clean granulating surfaces. They are cut, applied, and dressed by any of the accepted methods. The initial dressings are changed at about the eighth day.

We have used this technic on two extensively burned patients. In the case which is summarized below, two early débridement and grafting operations

were done on the 15th and 24th days, respectively. The result of the first operation is shown in Figures 1 and 2. Due to these early operations this patient had almost one-half of his wound already grafted by the fifth week, the time when, in most cases, grafting is just to be started.

Case Report.—C. R. A 40-year-old mechanic's clothes caught fire, producing a complete third degree burn from ankles to gluteal folds. He was admitted to the hospital

FIG. 1

FIG. 2

FIG. 1.—Showing result of sharp débridement of posterior surfaces of legs on 12th day.
FIG. 2.—Showing the healthy appearance of initial grafts when dressed nine days after their application.

on June 30, 1943. The burned areas were superficially débrided, lightly washed, and dressed with vaselined gauze and thick pressure dressings. He received plasma continuously for the first 30 hours and frequent whole blood transfusions thereafter, as indicated. The primary dressings were changed on the 15th day. At this time, sharp surgical débridement of part of the wound was carried out under ether anesthesia, with the result shown in Figure 1. Four split grafts of about $1\frac{2}{1000}$-inch thickness were then cut by dermatome from the back and sutured in place under slight tension. The grafts and surrounding burns were dressed with sulfanilamide powder, vaselined gauze and pressure dressings. These dressings were first removed nine days later. The grafts were found to have taken almost completely (Fig. 2). Further débridement was then carried out under anesthesia and

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more grafts were cut from the abdomen and applied to the anterior surfaces of thighs and legs. This second grafting was on the 24th day. These grafts were dressed by the same method. More split-thickness grafts were applied on the 39th day. The pat'ent was discharged on his 140th day, November 16, 1943, completely healed, after several minor pinch-grafting procedures.

FIG. 3
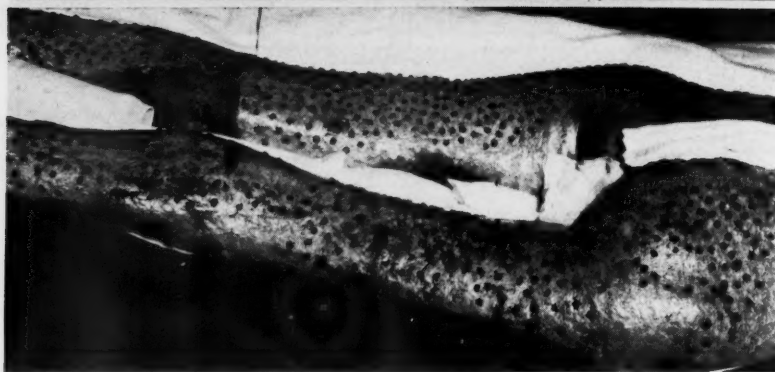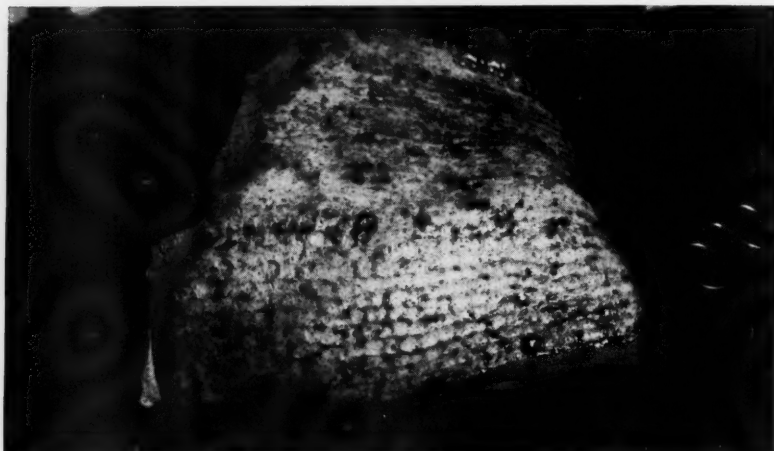
FIG. 4

FIG. 3.—Showing the small donor site of right shoulder from which 850 grafts were removed on the 30th day.
FIG. 4.—Showing the 850 grafts in place on the day of operation. The anterior surfaces had been grafted ten days earlier.

MASSIVE PINCH-GRAFTING

An occasional patient with full-thickness burns of 50 to 60 per cent of the body surface will survive long enough to become a serious and difficult problem in skin grafting. The extensive areas must be rapidly covered if a slow down hill course, with eventual death, is to be avoided. These patients do not have large enough areas of normal skin to serve as donor sights for split-thickness grafts. Homografts may be used and, at times, may be life-saving, but in general they are unsatisfactory as they serve only as a temporary covering for the wound.[4] Thus pinch-grafting often must be used in these cases.

In order to save life massive transference of skin must be undertaken as early as possible.

The usual deep pinch or Davis graft is full-thickness at its deepest point. The usual technic of cutting the grafts leaves normal skin between the individual donor holes. We have altered this procedure in that we use small grafts of less than one centimeter in diameter. They are cut superficially so that only an occasional pin point area of fat appears through the remaining layer of dermis. No normal skin is left between holes on the donor site. The small donor area heals rapidly and without the usual pock-marked appearance of pinch graft donor sites. It eventually becomes almost as smooth and even in appearance as an area from which a thin split graft has been taken. With this modified technic a very large number of small grafts may be taken from the relatively small donor area. Since each small graft spreads new epithelium from its whole periphery and since, with the large number of grafts, they may be placed quite close together, relatively rapid healing of large areas may be obtained. In the case reported 850 individual grafts were taken at a single operation from an area about eight inches square. They were applied to, and adequately covered, the buttocks and posterior surfaces of both legs.

Case Report.—D. B. A 60-year-old, emaciated, colored woman's house coat caught fire. She received extensive full-thickness burns of legs, buttocks, perineum, back and arms—a total of about 60 per cent of the body surface. She entered the hospital 12 hours later, on August 28, 1943, at which time she was in shock. She received plasma continuously until the 30th hour. The wounds were dressed with vaselined gauze and pressure dressings. Pinch-grafting was started on the 25th day, by which time only a few small areas about the perineum were in condition to receive grafts. The anterior surfaces of the thighs and legs were covered with about 450 grafts on the 32nd day. On the 38th day 850 grafts were taken from the shoulder area and applied to the buttocks and posterior surfaces of thighs and legs. About 90 per cent of the previously placed pinches were found in healthy condition. Figures 3 and 4 show the relatively small donor area and the appearance of the grafted surfaces at the completion of the second operation, which was carried out under local anesthesia with small amounts of adrenalin added as a hemostatic agent. Despite frequent blood transfusions and the best supportive measures the patient died on her 48th day, October 15, 1943. The final group of grafts appeared to have taken very well when examined two days before death.

SUMMARY

Two modified technics of skin grafting have been presented. They have been found to be of assistance in the care of patients with extensive deep burns.

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FURTHER EXPERIENCE WITH THE TREATMENT OF BURNS WITH SULFONAMIDE-IMPREGNATED MEMBRANES

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SINCE THE PRELIMINARY REPORT[1] of the local treatment of burns with chemotherapeutic membranes the discussion and experimentation which were then being carried on with this and other methods have become even more extensive. As more experience has been gained in the handling of large numbers of burns under the stress of military or naval action, or in civilian catastrophe, the need for modifying technics to fit individual situations has become evident. Thus, it is recognized that what may be an "ideal" method of treatment in a civilian hospital, where the patient can be retained under close observation throughout whatever period is required and where sufficient personnel for elaborate routines is available, does not fit the exigencies of burn therapy near the front or aboard ships in action. A wide range of technics continues to be employed though the National Research Council has recommended the use of a bland ointment locally and sulfonamides by mouth. While such a method may have the advantage of simplicity and suitability to wide application by personnel of varied degrees of experience, it is still subject to criticism.

Since the initial report of ten cases we have continued to treat all burns with a sulfonamide-impregnated plastic film.* The plastic employed is methyl cellulose and the sulfonamides—20 per cent sulfanilamide and 10 per cent sulfacetamide—are buffered to a p_H of about nine, at which Schmelkes, and his associates[2] have shown these drugs to be most effective. The film is light, strong, and when applied to a "weeping" surface, or otherwise moistened, adheres readily to its contours. The present report deals with an additional 57 consecutive cases of burns treated in the New York Hospital.

The routine treatment was as follows: In every instance shock was considered the matter of first concern and was treated in the usual manner, including plasma as required. When this was under control the local lesions were examined and simple débridement carried out in the accident room, but

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* The film is manufactured and supplied by the Wallace & Tiernan Products, Inc., Belleville, New Jersey.

under sterile precautions. This consisted merely in opening blebs and lifting off any detritus but not in any extensive operative procedure.

The therapeutic membrane was then applied, either in strips or in sheets, as best adapted to the area involved, and in such a manner as to come into close contact with the burned area. In very moist areas more than one layer of the film was applied at the time of the original dressing and vaselined gauze was used in a few cases after the film was in place as a means of further sealing the dressing. For the most part, however, simple dressings of gauze sufficed and in all cases were covered with pads and so bandaged as to produce a moderate and even pressure over the involved area. In children a light layer of plaster was frequently used both for immobilization and to maintain the dressing in place.

The dressing was changed only when necessary and in many instances a single application of film was all that was required. In the more severe cases the outer dressing was removed and the burn inspected through the transparent film. It was noted that the membrane underwent one of three changes—it became dissolved by the fluid from the surface of the burn; it became dry and flaked into small pieces; or it remained dry, intact and following the contour of the area. If necessary, new film was applied over the old and recovered as before or, as in a few instances there was an accumulation beneath the film, it was completely removed and fresh reapplied. When an area was completely healed the remaining film was peeled away, soaking the more adherent areas with moist sponges.

Bacterial Studies.—Numerous cultures were made from the burned areas both at the time of the first and of subsequent dressings. Positive cultures were frequent throughout the period of treatment but in only two cases were clinical signs of infection present in connection with second degree burns and one of these was a patient who had been burned six days previous to her entry into the hospital. All third degree areas showed growth on culture and generally obvious infection until healing took place.

The most common organism found was *Staphylococcus aureus,* while more rarely *beta* hemolytic streptococcus, nonhemolytic streptococcus *gamma,* diphtheroid bacilli, *B. proteus, B. subtilis* and *Cl. welchii* were encountered.

The film, through gradually liberating sulfonamide as it is dissolved, exerts a definitely bacteriostatic effect but cannot be considered as actually sterilizing the burned area. Indeed, a rather frequent finding beneath the film was a membrane of fibrin which, on microscopic examination, contained enmeshed leukocytes and some bacteria. The presence of this membrane was a source of some concern at first but as it became apparent that epithelization continued beneath this and that healing was not retarded, its removal was not considered necessary. Such a fibrin membrane may, in fact, be a part of the healing process in burns since we have found it present in experimental human burns treated by other means, such as with bland ointment and pressure dressings.

RESULTS

The age of the 57 patients included in this report ranged from nine months to 73 years, and the burns were all of thermal origin. Two cases, both infants with burns of over 70 per cent (Berkow's method) of the body surface, died within 48 hours of admission. Almost all of the burns appeared on inspection to be of second degree severity, but our experience with another method of determining this point[3] leads us to feel that many small areas in which the epithelium is completely destroyed may be present in what appears to be a pure second degree burn.
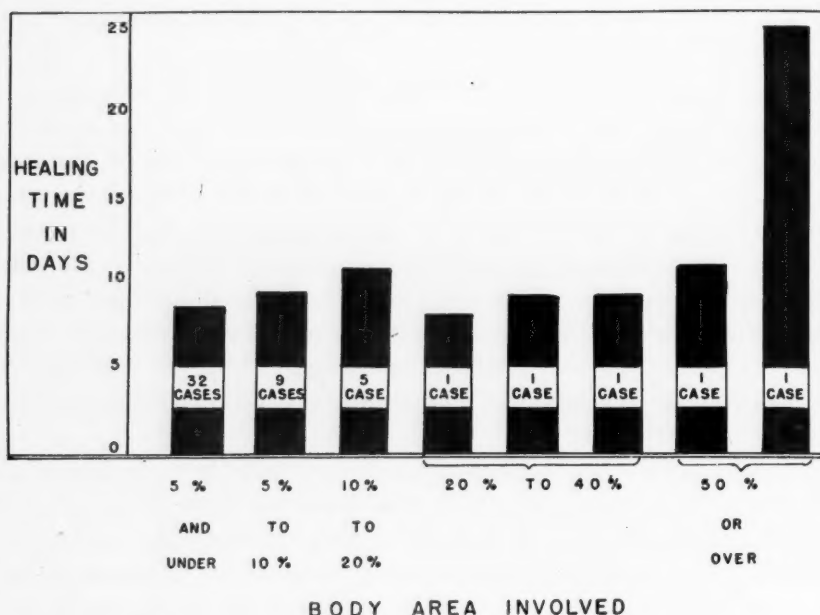
FIG. 1.—Graph showing the healing time of second degree burns.

Thirty-two of the series involved 5 per cent, or less, of the body surface, and these had an average healing time of 8.4 days, the extremes being four and 16 days respectively—the latter representing a single exception. Burns involving 5–10 per cent of the body surface numbered nine, all of which healed in almost exactly nine days. In five patients the burns involved 10–20 per cent of the body surface and these healed on the average in 11 days. There were three patients with burns involving 20–40 per cent of the total body area and which healed in eight, nine and nine days, respectively, and two cases with 50 per cent, or more, of the body surface burned which were completely healed in 11 and 25 days. Although the burns were widely distributed over the body, we were unable to correlate the speed of healing with any given part except the face, where epithelization is uniformly faster.

COMMENT.—Reference to Figure 1 reveals the fact that in this series with the exception of a single case, the size of the burn bears little relation

to the time required for healing. The most obvious explanation would seem to be that epithelization takes place from multiple foci, such as the cells about the base of hair follicles which, being relatively evenly spaced over a given region, become connected in about the same length of time regardless of the total area involved. The aim of therapy of such burns should, therefore, be to facilitate the operation of this mechanism as much as possible. To this end the mode of treatment should be of such a sort as to avoid mechanical or chemical injury to the remaining viable tissues as well as to control infection, since these are the chief hindrances to healing.
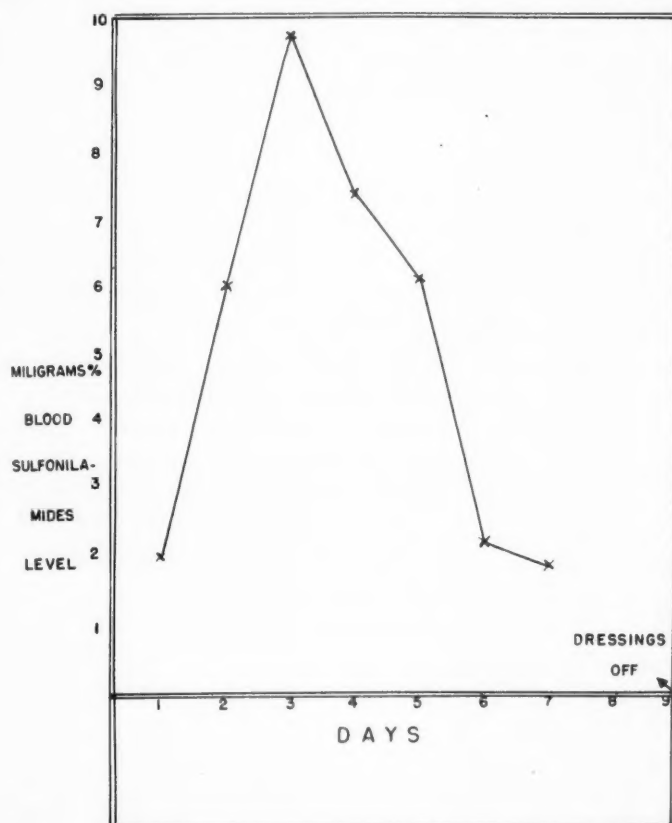
FIG. 2.—Graph showing highest blood sulfonamide levels from local absorption in this series. The patient was an infant with burns of more than 50 per cent of the body surface. Note the fall of blood levels as healing progresses.

All burns are contaminated in their early stages but gross infection is usually absent so that strong antiseptics are not required. All that is needed is a bacteriostatic agent and a means of preventing further contamination. For this purpose the Subcommittee on Surgical Infections of the National Research Council and the Contaminated Wound and Burn Project under the Committee of Medical Research of the Office of Scientific Research and Development[4] have recommended the employment of a bland ointment locally

and the administration of sulfonamides by mouth. While this may be a simple and most useful treatment in the field, we do not feel that it is the ideal mode of therapy since in our experience it is associated with a definitely longer healing time than some other methods.

It is these very criteria plus the great ease of application which brought about the development of the chemotherapeutic membrane. During our own experience with it the film has been improved by varying its composition. At present it is .004 inches thick and is constituted as follows: The base is methyl cellulose-triethanolamine to maintain a p_H of about 8.5, and the sulfonamides employed are 20 per cent sulfanilamide and 10 per cent sulfacetimide. One square centimeter of the film contains three mg. of sulfonamide. The choice of the ingredients is dictated by a number of factors and the p_H is adjusted to that point at which the maximum activity of the contained sulfonamides is reached.

No ill effects have been noted from the use of the film and although three patients had previously had local application of sulfonamides, no allergic manifestations have been observed. The local liberation of sulfonamide from the film is readily demonstrable since measurable blood levels have been obtained. These have usually been quite low and in proportion to the area involved, but in one patient, an infant with more than 50 per cent of the body surface burned, a maximum of 9.7 mg. per cent was reached. (Fig. 2.) There seems to be a gradual liberation of the drug from the film and absorption into the blood stream.[5] Despite a relatively uniform supply available in the film, which may be renewed at intervals, the blood levels tend to fall as healing progresses, and, indeed, the curve of such levels constitutes a fairly accurate index of epithelization.

Other striking features of this method are the rapid relief of pain and the relative speed with which the burn surface ceases to weep and becomes dry. While no comparative figures are available, we have been impressed with the relatively smaller amounts of plasma required to restore the normal hematologic relationships in film-treated cases.

Third Degree Burns.—In this series we confirm the impression of others that third degree burns are long in healing by any of the ordinary methods and to this sulfafilm is no exception when used as the sole definitive treatment. Thus, in 11 cases the average healing time was 44.2 days. Such burns involve necrosis, sloughing of tissue, infection and granulation, with healing either by spontaneous and slow epithelization or delayed grafting. It is commonly held that third degree burns often require 30 days to be prepared for grafting.

Recently we have used a test devised by one of us[3] by means of which it is possible to determine at any time what area of a burn is second degree and what third degree. This consists of the injection of sodium fluorescein (10 cc. of 20 per cent solution) intravenously and the illumination of the area with ultraviolet light. When this is done the second degree areas stand out as brilliant yellow in color while those of third degree are dark purple

A. On admission.

B. On third day after admission.

C. On seventh day after admission.

D. Twelfth day—patient discharged.

PLATE I.—Case W. D. Patient was a 23-year-old colored man who came in contact with a high tension wire and sustained a severe flash burn over 35 per cent of body surface (Berkow). The burn involved chest, face and neck, back and arms. Tannic acid spray was applied in the emergency room, consequently complete initial débridement was not possible until third day although film was used from the outset as definitive therapy. Patient's shock responded well to plasma therapy. He was out of bed on seventh day and discharged on twelfth day.
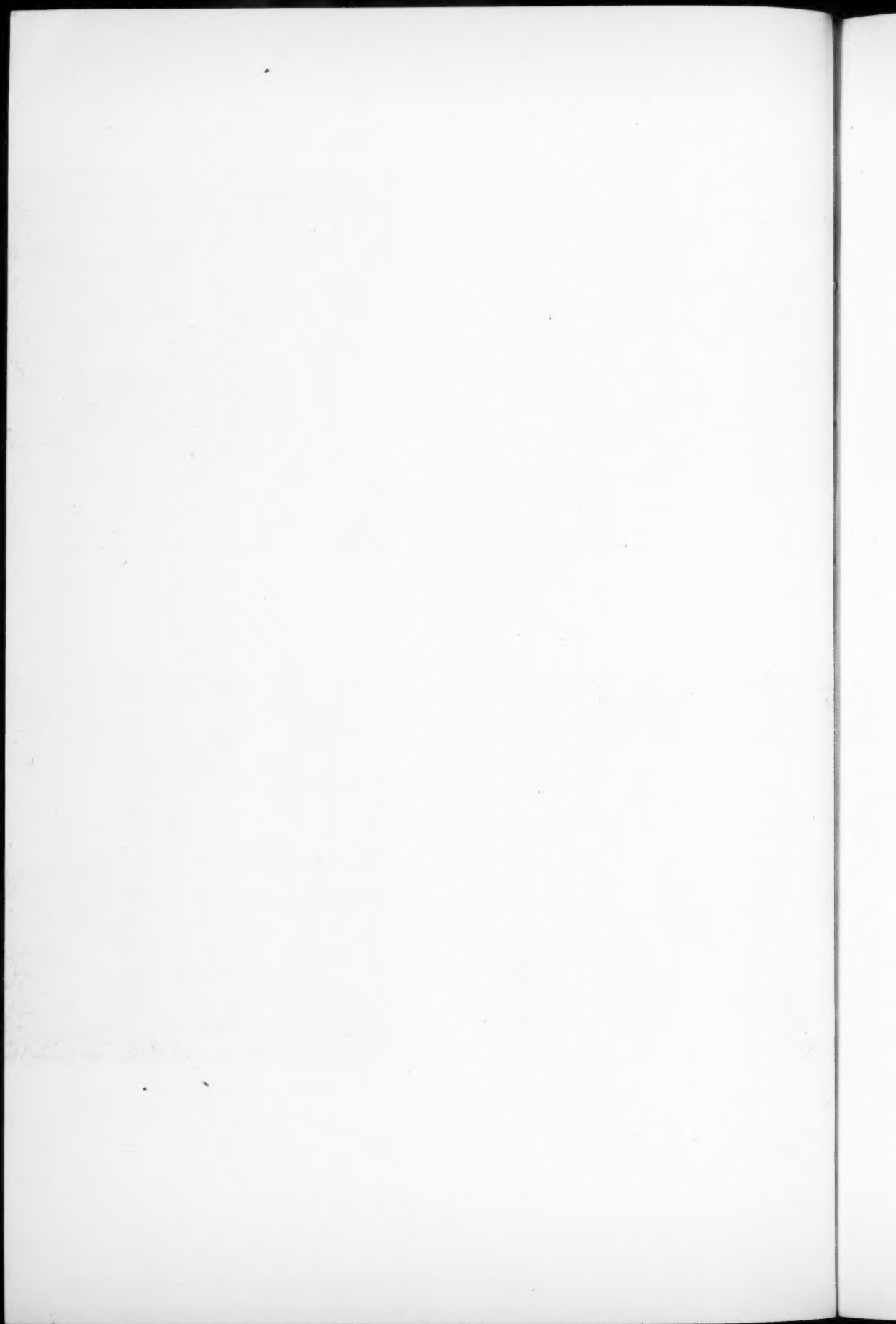
or black. Using such a test it is possible to excise third degree areas within a few days of their inception and by immediate grafting to shorten materially the time required for complete healing.

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PRIMARY HEMANGIOMATOUS TUMORS OF SKELETAL MUSCLE

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THE PURPOSE of this paper is to present a comprehensive survey of primary hemangiomatous tumors of skeletal muscle, with a complete analytic review of the literature to date. This is preceded by reports of two cases of our own, one most unusual and the other ordinary, for comparison.

The main features of the first case are those not commonly encountered, and are as follows: A 35-year-old woman noted over a period of five years, on the lateral aspect of her left thigh, a slowly growing mass which pulsated, had a bruit, and was unassociated with any symptoms except slight pain shortly before admission. Temporary ligation of the left common iliac artery was performed to minimize bleeding. A partially circumscribed hemangio-endothelioma, involving three contiguous muscles, was then widely excised. Postoperative deep roentgenotherapy was given. Complete recovery ensued, without any loss of function.

CASE REPORTS

Case 1.—Y. D., white, female, age 35, was admitted to Doctor Shallow's private service at the Jefferson Medical College Hospital, September 21, 1942, referred by Dr. George Miller of Norristown, Pa. The chief complain was a swelling in the left thigh.

In August, 1937, about three months after the delivery of her only child, the patient noticed that her left thigh, on the upper lateral aspect, was slightly larger than the opposite thigh. Doctor Miller, at that time, could find no demonstrable cause for the enlargement. During the next four years the disproportion increased gradually until a definite mass became visible. In December, 1941, on one occasion, and for the first time, the patient experienced a dull diffuse pain in the left thigh and leg following exertion. A roentgenogram revealed no bony abnormality, and it was thought that the patient might have a "fatty tumor." In September, 1942, the patient again experienced the same type of pain as noted previously, and thereafter it persisted as a dull, nagging discomfort aggravated by exertion. Because of this symptom she again consulted Doctor Miller, who noted a distinct, pulsating mass for the first time.

Systemic review was normal except for the symptoms as elaborated pertaining to the mass. Her general health was excellent and her weight remained unchanged.

Past history, especially as regards previous trauma, revealed a fall on the ice in 1935 and a fall from a horse in 1936, with trivial injuries not related to the left hip. Her obstetrical record revealed the application of low forceps, with a resultant second degree incomplete vaginal tear, treated by primary repair. The puerperium was normal. An operation was performed in December, 1940, for removal of a stone from the right ureter. The family history was irrelevant.

Physical Examination.—Temperature, pulse, respirations, and blood pressure were

normal. Weight 114 lbs. Except for a right inguinal operative scar the positive physical findings were confined to the upper lateral aspect of the left thigh. On inspection, there was present a large spindle-shaped mass extending from the anterior superior iliac spine to the junction of the upper and middle thirds of the left thigh, and about four inches at its maximum width. A few slightly dilated superficial veins were visible through the overlying skin which was freely movable over the mass. It was smooth, firm, difficultly compressible, nontender, and slightly movable. An expansile pulsation was present throughout the entire mass, and over it a systolic bruit could be heard, loudest over the junction of the mass with the femoral artery. The main bruit could be silenced by compression of the femoral artery in the groin, which caused a slight decrease in the size of the mass. However, in the upper left gluteal area there persisted a soft, systolic murmur (Fig. 1). No thrill was palpable. Branham's test was negative. There was no edema of the left leg, and the pulsations of the popliteal, posterior tibial, and dorsalis pedis arteries were palpable and equal on both sides.

Area of persistent murmur
despite compression of Femoral
Artery at groin, due to supply
by Gluteal Vessels.
(Also observed by Dr Matas)

Area of murmur
silenced by compression
of Femoral Artery at groin
(Intensity of stippling indicates
intensity of murmur)
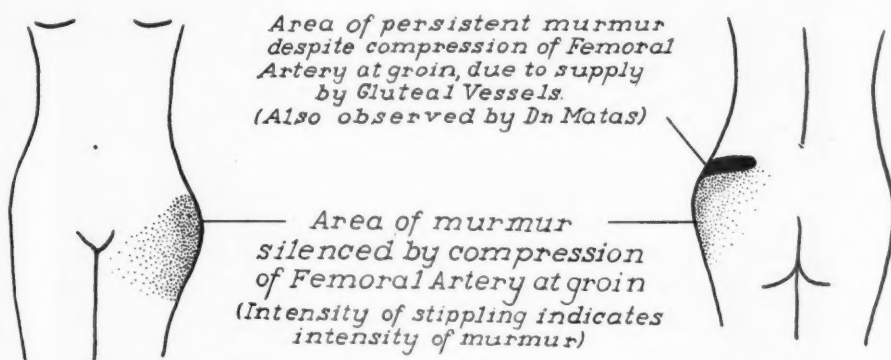
FIG. 1.—Diagram indicating distribution of murmur.

Laboratory and Special Studies.—The patient was studied at varying intervals during three hospital admissions. Blood count and uranalysis were normal. Wassermann and Kahn tests were negative. The electrocardiogram showed a conduction deformity suggestive of mild myocardial change. Roentgenograms of the lung fields and heart were essentially normal, and those of the left femur and hip were negative for bony abnormality or vascular calcification, but there was an alteration in the soft tissue structure detail in the area of clinical interest (Fig. 2). Arteriography by injection of thorotrast, both into the femoral artery and tumor mass itself, failed to outline the lesion satisfactorily.

The patient was seen in consultation by Dr. Rudolph Matas, who, following careful study of this case, with repetition of many of the studies previously made, including arteriography, concluded that the lesion was a diffuse aneurysmal tumor, almost exclusively arterial, supplied largely by the femoral artery (probably 95 per cent) and the gluteals (barely 5 per cent). He believed that it could be designated as a progressive neoplastic nonmalignant angioma-arteriale cavernosum (not a cirsoid in an arteriovenous sense).

In view of the type of lesion suspected preoperatively, both from our own studies and those of Doctor Matas, it was decided that primary extirpation was the procedure of choice. The patient well understood the risk involved and granted permission for a hip joint amputation, should this be necessary.

Operation.—January 21, 1943: Doctor Shallow. Open-drop ether anesthesia. In order to minimize bleeding, the left common iliac artery was temporarily ligated by two turns of tape clamped with a hemostat retroperitoneally through an inguinal incision.

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A longitudinal incision 11 inches in length was then made over the mass, starting at the level of the iliac crest. Within and beneath the tensor fasciae latae muscle, involving also the vastus lateralis and gluteus maximus, was a firm, rubbery, oval mass about 12 cm. in length and 8 cm. in width. It was densely adherent to the surrounding tissues, rendering separation impossible except with the scalpel. Beginning at the lower pole each large vessel was exposed, cut between clamps and ligated. The medial edge of the mass was then exposed, at which site the main supply was encountered. The

FIG. 2.—Roentgenogram of thigh (during arteriography) nine months after onset of pain, showing increased depth of soft tissue shadow lateral to greater trochanter.

vessel, representing the lateral femoral circumflex, was about the size of the normal femoral artery. In addition, there were numerous smaller collaterals. Since the common iliac artery was shut off by the tape, no thrill was felt, nor were any pulsating veins seen. The medial edge was freed to just below the iliac crest. Then the deep aspect of the mass was freed, at the posterolateral border of which several large blood vessels were encountered. These were divided between hemostats and the mass could then be turned upward. At the upper pole numerous large blood vessels were ligated and the mass then cut free near the anterior superior spine.

After removal of the tumor, many dilated blood vessels were noted on the sheaths of the gluteus maximus and tensor fasciae latae muscles. The fascia and muscles
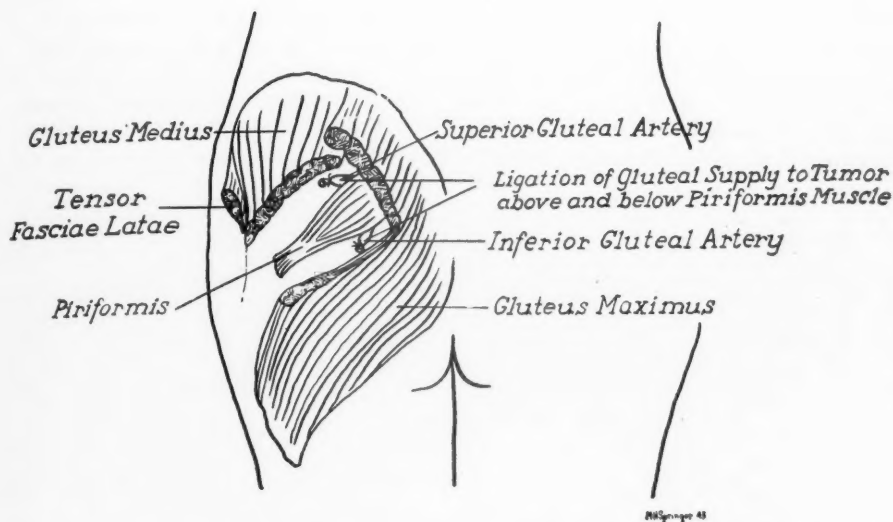
FIG. 3.—Sketch showing extent of excision of tumor and ligation of gluteal vessels above and below the pyriformis muscle.
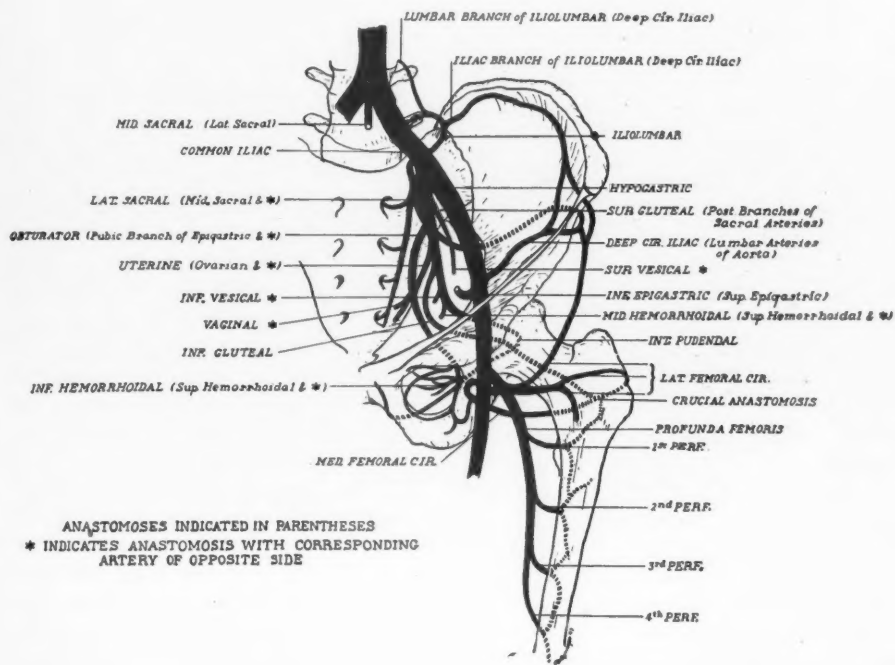
FIG. 4.—Diagram indicating collateral circulation following ligation of common iliac artery.

containing these were removed up to the upper pole of the cavity outlining the removed tumor mass. At this area several large blood vessels were encountered leading posteriorly. These were followed through the gluteus maximus and medius to the pyriformis muscle. Here they were ligated and divided (Fig. 3) above and below the pyriformis (superior and inferior gluteal vessels, respectively), and the muscle mass (tensor fasciae latae and part of the gluteus maximus and medius) removed (Fig. 7). Troublesome bleeding then occurred at the upper pole, even though the common iliac artery was shut off, due to collateral circulation (Fig. 4). This was controlled by ligation of several large vessels.

FIG. 5.—Gross specimen consisting of tumor and adjacent muscle.

The tape around the common iliac artery was next removed, followed by bleeding from many capillary areas, readily controlled by continuous catgut sutures in the adjacent muscles. Sulfanilamide (8 Gm.) was placed in the two incisions, both of which were closed without drainage. Approximately 400 ties (80 tubes of catgut) were employed for ligation of the vessels. During the operation (total time exactly three hours) the patient received 16 Gm. of plasma and 1200 cc. of whole blood, and remained in fair condition.

Pathologic Report.—The specimen (Figs. 5 and 6) consists of a partially circumscribed, fusiform, moderately firm mass, measuring 10 cm. in length and 5 cm. in diameter. It is composed of numerous bundles of muscle interspersed between which there are wide streaks of yellowish-gray tissue containing scattered large and small thin-walled blood vessels. The tumor is homogeneous throughout and contains no areas of necrosis or hemorrhage. The second specimen consists of two pieces of red muscle. the larger of which (Fig. 7) measures 13 x 9 x 3 cm. They are not permeated with yellow tissue as in the first specimen and are covered with a fibrous tissue sheath about 1 Mm. thick, containing several dilated tortuous thin-walled blood vessels.

Microscopic examination shows many small caliber vascular channels in a fibrous and fatty tissue stroma, and degenerating muscle bundles at the periphery (Fig. 8). In

other areas (Fig. 9) there is very marked proliferation of the capillaries, with hyperplasia
of the lining endothelial cells. *Pathologic Diagnosis:* Hemangio-endothelioma, cavern-
ous type.

Postoperative Course.—During the first six days the patient received 2,000 cc. of
whole blood and 48 Gm. of plasma intravenously. Thereafter, the hemoglobin and red
cell count gradually rose to normal levels, aided by high caloric, high protein diet and

Fig. 6
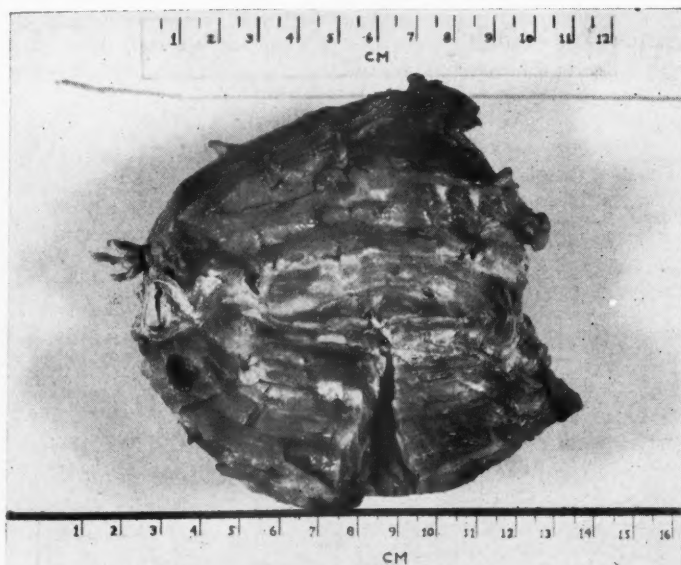
Fig. 7

Fig. 6.—Cut-section showing replacement of muscle bundles by tumor tissue.
Fig. 7.—Muscle mass adjacent to tumor containing dilated vessels of supply.

adequate doses of ferrous sulfate and vitamins B, C, and K. The inguinal incision
healed by primary intention, but the thigh incision became infected and discharged
small pieces of catgut and pus (positive for *Staphylococcus aureus*). Following irriga-
tion therapy with sulfanilamide solution, the temperature became normal by the end

of the second week. At this time the patient was able voluntarily to flex the knee and thigh almost fully.

On the 35th day the patient was allowed out of bed, and by the 38th day could walk several steps unaided. At this time there was complete absence of the previous mass, pulsation, and bruit. Examination by Dr. David Kramer, from the Department of Peripheral Vascular Disease, revealed that the femoral pulses were fair on both sides and posterior tibial and dorsalis pedis pulses good on both feet. The oscillometric readings were: 3° to 3½° spikes in the thighs (normal 6° to 10°); 2½° spikes in the legs on either side (normal 5° to 8°). The histamine test was somewhat delayed on the right side, but more definitely delayed on the left foot and leg as well as a slight delay in the thigh. The skin surface temperature readings were:

	Right	Left
Big toe (dorsum)	24.5°	27°
Middle toe (dorsum) ...	23.3°	23.8°
Sole	26.8°	26.2°
Dorsum of foot	27.5°	28°
Leg	30°	30°
Thigh	20°	29°

These studies of circulatory function indicated some impaired circulation bilaterally, more so on the left, most likely due to arteriospasm.

The patient was discharged April 6, 1943, on the 75th day postoperatively. Because of the possibility of malignancy, as suggested by the histologic section, the operative field on the thigh was further treated by roentgen irradiation, given in doses of 200 r. daily during a period of three weeks from June 29, to July 20, 1943. When last seen on January 20, 1944, one year after operation, the patient appeared in excellent general health, her gait was essentially normal, and the incisions were well healed.

The main features of the second case are those more commonly encountered, and are as follows: A ten-year-old boy noted on the inner aspect of his right arm following trauma, a lump which within six months increased in size and became painful. Physical examination revealed a soft, tender, walnut-sized mass over which a bruit could be heard. A cavernous hemangioma involving the medial head of the triceps muscle was removed at operation. During the next two years a mass, representing recurrence in the long head of the triceps, gradually appeared on the posterior aspect of the arm, accompanied by pain and limitation of extension of the forearm. It was widely excised, followed by primary wound healing and complete restoration of function.

Case 2.—V. S., white, male, age ten, was admitted to the Children's Ward, Jefferson Medical College Hospital April 4, 1941, with the chief complaint of a painful swelling on the inner aspect of the right arm. In October, 1940, the patient first noticed the lump following a blow. During the ensuing months the lump, which originally was pea-sized, increased gradually to the size of a walnut and was accompanied by a continuous, dull pain, aggravated by use of the arm. The past medical history and family history contributed nothing of significance.

Physical Examination.—The vital readings were normal, and the positive physical findings were confined to the right arm. On the inner aspect at the middle third there was visible a mass about the size of a walnut, with normal overlying skin. It was soft, easily compressible, lobulated, and tender on palpation. No pulsation or thrill were felt, but a systolic bruit could be heard on auscultation. Branham's test was negative.

Laboratory Data.—The blood count and uranalyses were normal. Wassermann and Kahn serologic studies were negative. Roentgenograms of the arm revealed no bony abnormality. Arteriography was unsatisfactory. *Diagnostic Impression:* Arteriovenous hemangioma or possible congenital arteriovenous aneurysm.

Operation.—April 15, 1941: The first operation was performed under open drop ether anesthesia. A longitudinal incision about six inches long was made on the medial surface of the right arm, exposing an angiomatous mass involving the medial head of the triceps muscle. The main vessels of supply were from the profunda brachii, and these were ligated. About one-half of the body of the medial head of the triceps muscle, containing the mass, was resected. The fascia and skin were then closed without drainage. Pathologically, the lesion was reported as an angiomatous tumor of muscle.

Fig. 8.—Photomicrograph (× 50) showing vascular channels in a fibrous tissue stroma. Degenerating muscle fibers may be seen at the periphery.

Postoperative Course.—The wound healed by primary intention, and the patient was discharged as well on April 28, 1941, the 13th day postoperatively.

Subsequent Progress.—On March 10, 1942, a tender swelling posteriorly over the triceps muscle was noted. Biopsy revealed recurrence of the hemangioma.

Second Hospital Admission.—The patient was readmitted on April 5, 1943, at which time his general physical condition was again good and the physical findings limited to the right arm. The old healed scar of the first operation was present on the inner aspect of the arm. On the posterior aspect in the lower third was a soft, lobulated,

well-defined, oval mass, about 1 x 2 inches in diameter, which was moderately tender on palpation. Again, the overlying skin, except for the recently healed biopsy scar, was normal. There was no pulsation, thrill, or murmur. Complete extension of the forearm was limited about 30° because of pain. Blood count and uranalysis were normal.

Second Operation.—April 7, 1943: The patient was operated upon by Doctor Shallow, using nitrous oxide-ether anesthesia. A tourniquet was applied high on the arm. The incision was made over the mass and biopsy scar on the posterior aspect of
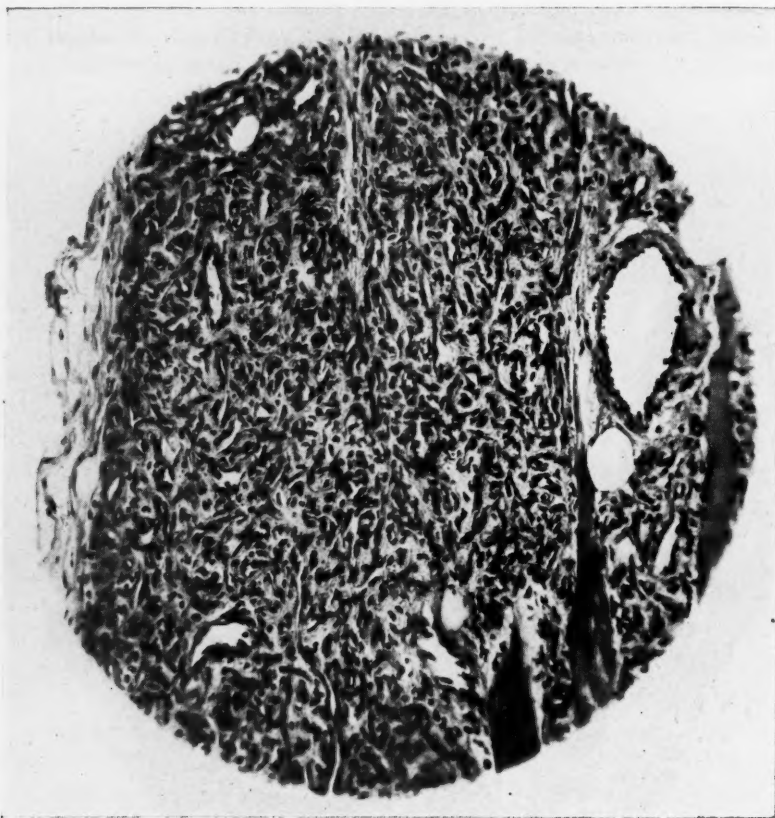
Fig. 9.—Photomicrograph (× 200) showing the endotheliomatous aspect of the lesion.

the arm so as to form an oval about 6 x 2 inches. There were no dilated vessels seen in the skin and subcutaneous tissue. Lying within the long head of the triceps muscle was an irregular, firm, infiltrating mass supplied by many moderate-sized, dilated vessels. These vessels extended into part of the tendon of the triceps muscle, and several reached the capsule of the elbow joint. The entire mass and all the dilated vessels were removed (Fig. 10). Most of the long head of the triceps muscle and part of the tendon were removed. Eight Gm. of sulfanilamide were placed in the wound, which was then closed without drainage.

Pathologic Report.—The gross specimen is shown in Figs. 11 and 12. Microscopically, the section is made up of loose fibrous tissue in which there are numerous blood vessels. Some of the blood vessels are fairly thick-walled, while others consist of cavernous spaces. In some areas there are giant cells. These appear to be foreign body type and

are about necrotic material which appears to be bone.   A representative area of the tumor is shown in Fig. 13.   *Pathologic Diagnosis.*—Hemangioma, cavernous type.

    Postoperative Course.—The wound healed by primary intention, and the patient was discharged on April 17, 1943, the 10th day postoperatively.   On January 20, 1944,

FIG. 10
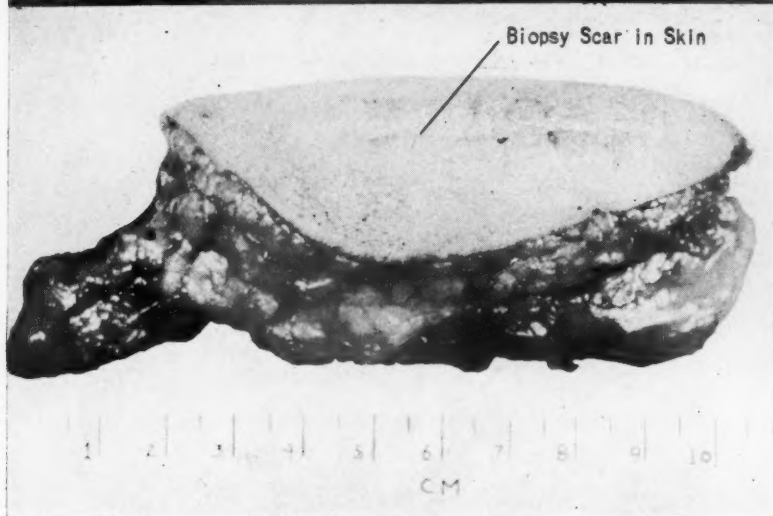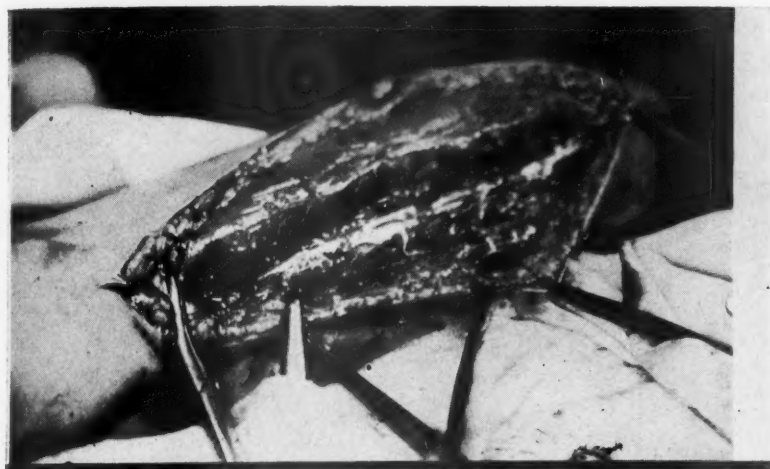
FIG. 11

FIG. 10.—Tumor and adjacent muscle tissue excised widely.
FIG. 11.—Specimen removed at operation.

when the patient was last seen, the scar was well healed, there was no evidence of recurrence, and extension of the forearm was complete, painless, and of essentially normal power.

For this study 335 cases of hemangiomatous tumors, primary in skeletal muscle, have been collected from the entire available literature, since the first reported case by Liston in 1843.   Of this number, 191 were taken from

Tumor Tissue

Tumor Tissue

Part of Triceps Tendon
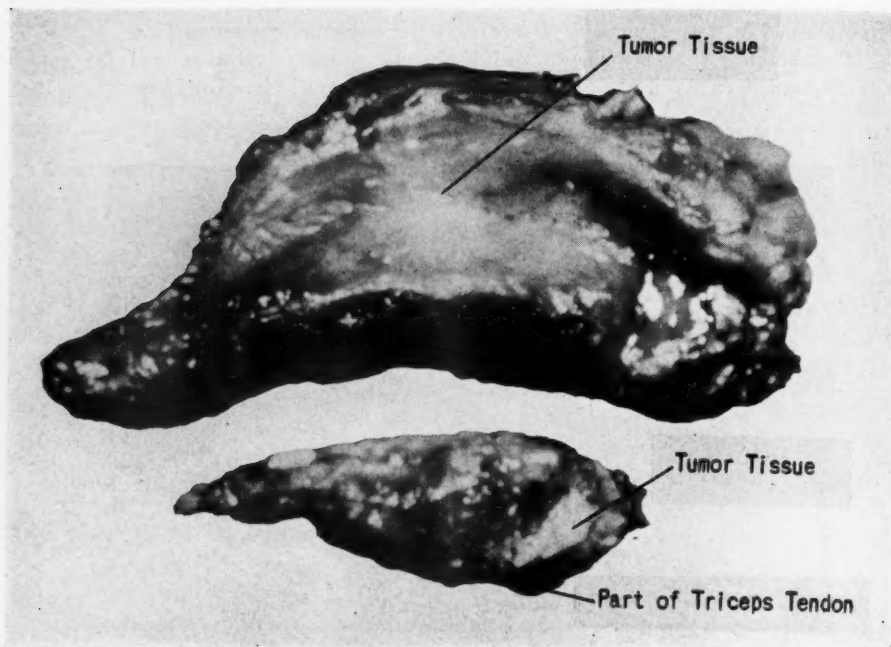
FIG. 12.—Gross specimen on cut-section.

FIG. 13.—Photomicrograph (×75) showing cavernous spaces in a loose fibrous tissue stroma.

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the review by Davis and Kitlowski in 1930. The 18 cases in the latter authors' series excluded by Jenkins and Delaney we have likewise excluded. In agreement with Weaver, we have, in addition, also excluded the first three cases of Eve, since it appears probable that these were primary in the synovia of the knee joint capsule. All of the 62 cases further collected by Jenkins and Delaney in 1932 we have included. Since that time we have been able to collect 80 additional cases from the world literature plus two of our own, summarized in Table IX.

DISTRIBUTION OF CASES
ACCORDING TO AGE GROUP AND SEX
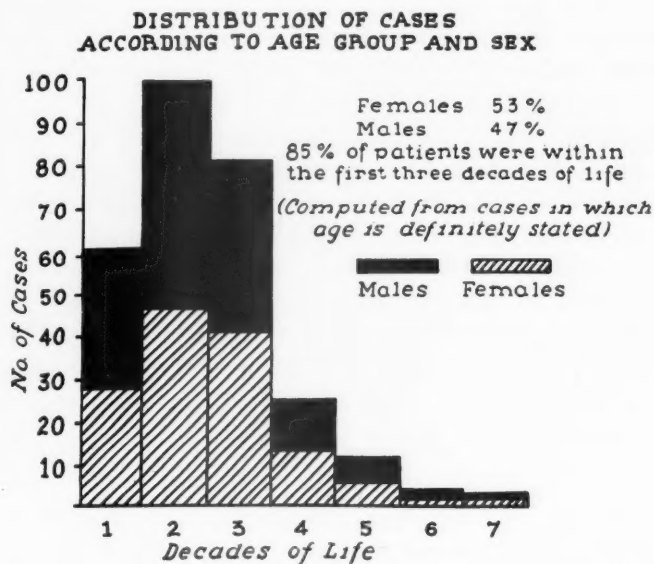
CHART I

Age and sex incidence.

The most complete reviews of this subject in the past are those of Sutter (1905), Davis (1908), Colli (1913), Mondor and Huet (1923), Davis and Kitlowski (1930), and Jenkins and Delaney (1932).

CLASSIFICATION

Hemangiomatous tumors comprise all those originating from blood vessels and their various components. Oughterson and Tennant classify these under three main divisions. The first group, or hemangiomas, consists of hemangiomatous malformations and hemangioblastomas. The second group is represented by angiomyoneuromas or glomus tumors; and the third group by Kaposi's hemorrhagic skin sarcoma. For the hemangioma group various authors have proposed classifications (Table I), but to date no single one has been universally accepted by both clinician and pathologist. In the present review, Muscatello's classification of hemangiomas has been adopted, because the greatest number of the pathologic reports fit conveniently into it. Further-

more, it is more differentiating than that of Boyd, Matas, and Fraser, and is more applicable to this study than that of Watson and McCarthy.

INCIDENCE

According to Kornmann, hemangiomas comprise 2–3 per cent of all tumors in the body and 7 per cent of all benign tumors. In a series of 1,308 hemangiomas (Watson and McCarthy), ten, or 0.8 per cent, occurred in skeletal muscle. In the present series the disease is almost entirely confined to the white race, except for seven Japanese (2.1 per cent) and three Negroes (0.9 per cent). Sex incidence is about equally divided, and the disease occurs predominantly (85 per cent) within the first three decades (Chart I).

Thomas has reported a case in which there were two tumors of the vastus internus muscle which had a histologic picture similar to that of a glomus tumor. The author, however, was not certain that these represented true glomus tumors. In our review of this case we concur with Light, who doubts the correctness of the diagnosis. Since glomus tumors in practically all instances arise in the stratum reticulare of the corium, and since to date there are no authentic cases arising primarily in skeletal muscle, this group of hemangiomatous tumors will not be further discussed. Kaposi's sarcoma is likewise omitted, since the lesions are not primary in skeletal muscle but originate in the derma.

TABLE I

CLASSIFICATION OF HEMANGIOMAS BY VARIOUS AUTHORS

General Classification of Hemangiomas

Author:	Boyd	Matas	Fraser	Muscatello	Watson & McCarthy
Classification...	1. Capillary	1. Capillary	1. Capillary	1. Capillary	1. Capillary
	2. Cavernous	2. Cavernous	2. Cavernous	2. Cavernous	2. Cavernous
		3. Plexiform	3. Compact	3. Venous	3. Angioblastic
				4. Arterial	4. Racemose
					5. Diffuse Systemic
					6. Metastasizing
					7. Nevus vinosus
					8. Hereditary Hemorrhagic Telangiectasis

ETIOLOGY AND PATHOGENESIS

To date there is no universal agreement concerning the etiology and pathogenesis of hemangiomas, and the following represent the various theories. The prevailing one is that hemangiomas are congenital tumors. As such their origin may be from abnormal embryonic sequestrations of vascular tissue which do not fit into the ordinary circulatory system and retain their embryonal characteristics (Cohnheim, Ribbert, Fraser, Ewing, Watson). Other views are that they may result from disease of the vasa vasorum (Virchow); simple

hypertrophy of vascular elements and not as a new growth (Rokitansky);
obstruction to blood flow (Sutter); increased vascular tension in the area
of formation of the tumor (Monzardo, Thoma); loss of support to small
vessels by atrophy of the surrounding connective tissue (Pupovac); or they
may represent vascular fibromas (Honsell). Heredity apparently plays no
rôle, since no two cases appeared in the same family.

A few authors (Pilzer, Lowenthal, Mailer) believe that trauma is a
primary factor. On the other hand, most authors agree that trauma plays
an important secondary rôle, both in the growth of the tumor and the
development of symptoms. In the present series trauma was reported as
related to the onset of the symptoms and signs in 17 per cent of the cases
(Table VII). The trauma may be external or internal (muscle action),
or a combination of both. In some instances the tumor was symptomless
for years, but became painful after a major injury or a series of minor ones.

Another factor playing a secondary rôle in inciting or aggravating symp-
toms, as stressed by Weaver, is the presence of systemic infection, as scarlet
fever (Kidner, Case 2), diphtheria (Weaver, Case 4), grippe (Guyot and
Jeanneney), appendicitis (Davis and Kitlowski, Case 6), pneumonia (Oi
and Yazaki), and the common cold (Fulton and Sosman, Case 1).

PATHOLOGY

Primary hemangiomas of skeletal muscle arise in the vascular plexus of
the muscle or in the perimysium between the muscle fibers. They represent a
dilatation and overgrowth of neoplastic vessels, as a rule benign in nature,
but which may at times assume malignant qualities. They differ from the
dilatations seen in varicose veins and the overgrowths in granulation tissue
and highly vascular tumors in that the latter represent the responses of
otherwise normal vessels to disease or to an increased demand for greater
local blood supply. When the demand ceases the vessels again may assume
normal size.

Grossly, the specimen often resembles a muscle containing varicose veins.
The color may be bluish due to thin-walled cavernous spaces protruding
between the muscle fibers. In some cases the color is reddish, yellowish, gray,
or a combination of these. The mass is usually moderately compressible, soft,
and spongy, but may be relatively hard and firm, as in the authors' Case 1.
On cut-section, whitish septa of fibrous tissue and remnants of tissue in
which the tumor developed bound communicating blood spaces. In some cases
the vessels may stand out like stems (Fig. 6). Muscle fibers are usually
entirely replaced by the tumor tissue especially at the center, but may be
present in various stages of degeneration peripherally. The hemangioma may
be sharply differentiated from the surrounding muscle or may gradually merge
into it. Thus pathologico-anatomically one may refer to circumscribed,
partially circumscribed, and diffuse types (Table II).

The circumscribed type was reported in 45 cases, or 13 per cent of the series. When this type possesses a distinct capsule (approximately half the cases), it seldom involves any structure other than the muscle itself, although in two cases the lesion was adherent to the periosteum and in two others nerves were damaged.

In the partially circumscribed type (16 cases, or 5 per cent), part of the tumor infiltrates the muscle and the remainder is distinctly separate, sometimes with a definite fibrous capsule. In three of these cases the tumor was adherent to the periosteum.

The diffuse type was by far the most frequent (131 cases, or 39 per cent). In the remaining 143 cases (43 per cent) the gross pathologic type was not mentioned. In the diffuse type there is an infiltration in irregular fashion of part or all of one muscle or adjacent muscles and other tissues with no sharp line of demarcation. Thus nerves were involved in 18 cases, subcutaneous tissue in ten, skin in three, periosteum and bone in 11, synovial membrane in seven, large arteries in six, and large veins in three.

Microscopically, the tumor consists of vascular elements (cavernous, capillary, venous, or arterial) in a connective tissue stroma (Table II). The predominating variety is the cavernous, although seldom do pure types exist. It is characterized by large, irregularly-shaped spaces filled with normal blood in a fibrous tissue stroma. The blood spaces usually have an endothelial lining but lack the definite walls of normal blood vessels. They communicate freely with each other and receive nutrition by means of their own arteries which empty into dilated veins. When large arteries are present, the satellite veins are often absent or else scarce. Mixed tumors may also develop in combination with fatty tissue (Keller), nonstriated muscle (Honsell), or lymph channels (Monzardo, Ritschl, Lucke).

The supportive tissue varies greatly in amount, thus determining the consistency of the tumor. Thrombosis, sclerosis, and hyalinization of dilated vessels may occur, followed by organization and laying down of dense masses of fibrous tissue. Fibroblastic proliferation may be so marked as to permit the diagnosis of sarcoma to be considered. In the stroma one finds remnants of striated muscle in various stages of degeneration. In the central part of the tumor the degenerative changes are complete, while towards the periphery the fibers are better preserved. Inflammatory changes are sometimes observed in the form of round cell infiltration or even at times as suppurating processes as a result of exogenous infection through injury. Rarely one may find ossified areas (Margarucci, Case 1; Kolaczek; Rocher and Uzac; authors' Case 2).

Blood calculi or phleboliths, varying in size from less than a millimeter to half a centimeter, may form at the periphery of the tumor where stasis is most marked. They consist of organized thrombi infiltrated with tricalcium phosphate, invested in a bed of endothelial cells and adherent to the vascular wall.

A cirsoid aneurysm may result from the development of free connections between the angioma and the arterial side of the circulation. When the angioma is freely connected with the venous side through veins with defective valves it is affected by mechanical changes in pressure.

Hemangiomas of muscle frequently remain inactive for long periods of time and then begin to extend rapidly with an invasiveness suggestive of malignancy. Growth is not by expansion as is usual in benign tumors, but by infiltration. The hemangioma invades the adjacent muscle fibers by multicentric proliferation of endothelial cells which subsequently form channels through which blood flows. The newly formed vessels and their supportive tissues compress the invaded muscle and its blood supply, resulting in atrophy and gradual replacement. This process becomes limited in the encapsulated circumscribed type. There is practically no tendency of the neoplastic vessels to anastomose with those already present in the invaded tissue. Indeed, the larger blood vessels may even be invaded, as in Case 2 of Kidner in which no posterior tibial artery could be found. In parts the tumor may be very cellular, as in the authors' first case (Fig. 9), and distinct vessels very scarce or not recognizable. Nerve fibers, when present, are usually resistant and appear normal microscopically, but the interior of a nerve trunk may become infiltrated (median nerve in the case of Huard). Bone may be affected secondarily by pressure of the adjacent tumor, resulting in atrophy; by increased blood supply, resulting in hypertrophy; and by irritation, resulting in periosteal proliferation.

The peculiarity of infiltration by a benign tumor, as just described, raises the question as to whether these tumors of muscle should be considered as potentially malignant, and whether metastases occur. Speaking of hemangiomas for all tissues of the body, Geschickter and Keasbey state that "an occasional angioma may metastasize following trauma or after repeated recurrences, but less than 1 per cent of benign angiomas subjected to treatment fall into this group." Malignant vascular tumors have recently been excellently reviewed by Stout. According to this author, hemangioendothelioma is the most common, type, characterized by the formation of atypical endothelial cells in greater numbers than required to line the vessels with a simple endothelial membrane, and the formation of vascular tubes with a delicate framework of reticulin fibers, showing a marked tendency for the lumens to anastomose. Silver staining of the vascular reticulin sheath causes the tubes to stand out in distinct relief. Stout has observed two cases* in which the tumor was primary in skeletal muscle. In one of them he reports the occurrence of evidence of lung metastases and symptoms of paraplegia four months after operation and death after seven months. Other authors have reported cases in which the tumor, histologically, has been regarded as

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* These cases appeared in the literature after the statistics for this article had been completed.

suggestively, or actually, malignant (Teller, Solis-Cohen, and Levine; Rives and Barras; Mauro; authors' Case 1).

<div align="center">TABLE II</div>

<div align="center">INCIDENCE OF THE VARIOUS GROSS AND MICROSCOPIC PATHOLOGIC TYPES</div>

<div align="center">Pathologic Types</div>

Gross	No.	Per Cent	Microscopic	No.	Per Cent
Diffuse	131	39%	Cavernous	182	54%
Partially circumscribed	16	5%	Capillary	11	3%
Circumscribed	45	13%	Arterial	8	2%
Not stated	143	43%	Venous	8	2%
			Mixed and unclassified	126	38%
Total	335			335	

SYMPTOMS, SIGNS AND SPECIAL STUDIES

Hemangiomas of muscle may be present for years, often from birth, without giving rise to symptoms of sufficient severity to cause the patient to seek medical aid. The duration of symptoms varied within the wide limits of one to 70 years, but was usually one to five years.

Pain is the cardinal symptom. It was definitely present in 200 cases (60 per cent), absent in 47 (14 per cent), and not stated in 88 (26 per cent). As emphasized by Weaver, there is no other small benign tumor which can be so excruciatingly painful as a hemangioma, except for the glomus tumor of Masson, which is somewhat similar in nature. Those located in long narrow muscles give rise to pain more frequently, since the spread usually exerts pressure on some nerve branch. On the other hand, wide flat muscles provide greater room for expansion before pressure on sensory nerves occurs. Congestion within the tumor as a result of trauma, obstruction by phlebolith formation, and growth within resistant surrounding tissues may be a significant secondary factor in the production of pain. Absorption of toxins from a distant focus might possibly explain those cases in which pain followed a previous infection.

The pain may vary from a dull ache and feeling of fulness, due to distention of the blood spaces, to a sharp radiating root-type of pain, often accompanied by protective muscle spasm, as a result of pressure on nerves from without or by inclusion of nerve elements in the tumor. It may be present only during the contraction phase, when muscle thickening causes nerve pressure (Mondor and Huet, Diedoff). There may be marked sensitiveness to touch (Kirmisson) and paresthesias such as numbness or formication.

A mass was present in 329 cases (98 per cent) and absent in six (2 per cent). It may be sharply demarcated or ill-defined and vary in size from a pea when first noticed (Serfaty; authors' Case 2) to a small pumpkin (Fritzsche) or fetal head (Honsell). It was described as tender in 105 cases (31 per cent), soft in 83 (25 per cent), hard in 68 (20 per cent),

<div align="center">716</div>

fuctuant in 23 (7 per cent), pseudofluctuant in 10 (3 per cent), elastic in 37 (11 per cent), and reducible in 26 (8 per cent).

In ten cases (3 per cent) a pulsation was noted, expansile in four (1.2 per cent), with a thrill in two (0.6 per cent) and a bruit in six (1.8 per cent).

Obicularis oculi 1
Obicularis palpebrae 1
Rectus internus 1
Inferior oblique 1
Eye—Cone of orbit 2
Temporalis 4
Masseter 15
Muscles of jaw not specified 1
Buccinator 1
Mylohyoid, geniohyoid, genioglossus 1
Sternocleidomastoid 6
Deep cervical muscles not specified 1

Deltoid 6

Pectoralis major 5
Serratus magnus 6
Intercostals 4
Biceps brachii 8
Muscles of chest wall not specified 2
Brachialis 1
Muscles of arm not specified 2
Abdominal muscles not specified 2
Diaphragm 1
Pronator teres 3
External oblique 3
Psous 2
Flexor pollicis longus 1
Rectus abdominis 6
Flexor digitorum sublimis 4
Internal oblique 1
Flexor digitorum profundus 4
Tensor fasciae latae 1
Sartorius 2
Volar and brachial muscles not specified
Thenar muscles 4
Adductor longus 1
Hypothenar muscles 1
Gracilis 2
Adductor pollicis 3
Muscles of hand not specified 1
Quadriceps femoris 16
Indiv muscles not mentioned
Rectus femoris 6
Vastus lateralis 13
Vastus intermedius 2
Vastus medialis 21

Peroneus longus 5
Tibialis anticus 3
Peroneus brevis 5
Extensor digitorum longus 1
Extensor hallucis longus 1

Peroneus tertius 1
Extensor digitorum brevis 2
Extensor hallucis brevis 2

CHART II
Incidence in individual muscles.

The presence of a pulsation may be accounted for by several factors. In the first place, it may merely represent a transmitted pulsation from a neighboring large artery. Second, it may represent the pulsation of an abundant arterial supply, for it is well known that very vascular tumors, as for example certain sarcomas, may pulsate. Hemangiomas are unique among tumors in that the tumor itself is composed of neoplastic vascular

elements which receive nutrition for growth from ordinary blood vessels, thus constituting two systems, one neoplastic, the other essentially normal. It is the belief of the authors that the pulsation of the tumor present in their first case was from the large arteries of supply from the deep femoral and gluteal vessels. The abundance of these vessels may be ascribed to the

Splenius capitis 2
Semispinalis capitis 1

Trapezius 12

Rhomboid 3
Subscapularis 1

Teres major 2
Infraspinatus 2

Triceps 20
Muscles of arm not specified 2

Serratus minor 3
Latissimus dorsi 12

Deep muscles of back not specified 2

Supinator longus 6
Extensor carpi radialis 1
Extensor carpi ulnaris 2
Muscles of arm not specified 11

Erector spinae 4
Lumbar muscles not specified 2
Sacrolumbar muscles not specified 2

Extensor pollicis 2

Gluteal 10
Gemellus 1

Interossei 2

Semimembranosus 13
Semitendinosus 6

Biceps femoris 16

Muscles of thigh not specified 2

Plantaris 1

Gastrocnemius 31

Calf muscles not specified 6

Soleus 17

Flexor hallucis longus 4

Flexor digitorum longus 3
Muscles of leg not specified 4

Tibialis posticus 1

Muscles of foot not specified 4
Abductor hallucis 1
Short muscles of sole not specified 2

Quadratus plantae and lumbricalis 1
Flexor hallucis brevis 1

CHART III
Incidence in individual muscles.

increased local demand for blood supply to a large, growing, unusually cellular hemangioma. The dilatation and hypertrophy of these vessels noted at operation may possibly be accounted for by the increased resistance to inflow of blood by the dense compressing fibrous tissue stroma. Third, the pulsation

may be from the neoplastic vessels themselves as in arterial angiomas, sometimes referred to as racemose, plexiform or arteriovenous hemangiomas (Picardi; Matsunami, Case I; Serra, Lavenia, and Frega).

In 22 cases (6.6 per cent) the tumor could be reduced in size by elevating the part. Increase in size or firmness was noted in 20 (6 per cent) on lowering the part or obstructing the venous return.

The overlying skin is usually normal, and was definitely stated as such in 132 cases (39 per cent). It was freely movable in 55 cases and fixed in seven. The skin was somewhat bluish over the tumor in 13 cases, telangiectatic in seven, contained dilated veins in ten, was atrophic in one, ulcerated in six, and contained naevi in two.

The area of predilection is the muscles of the extremities, particularly the lower (Table III), but any striated muscle in the body may become involved (Charts II and III). The thigh, especially the quadriceps femoris muscle, represented the most frequent site. The tumor usually involved only one muscle (66 per cent), but up to five or an en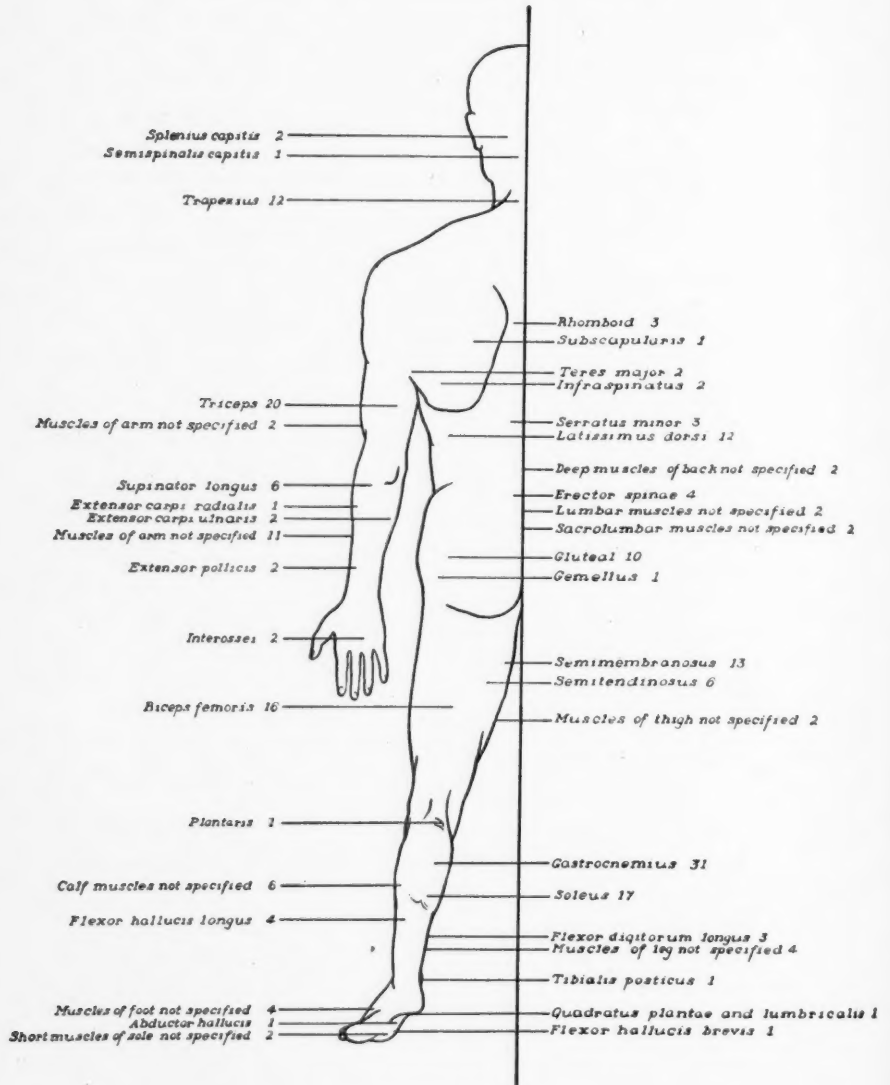tire group were recorded (Table IV). In five cases the tumors were multiple, that is involved noncontiguous muscles (Lichtenauer, Reboul, Poucel, Porcile, and Oi and Yazaki).

TABLE III
INCIDENCE AT VARIOUS SITES

Location*	No.	%
Head	26	7.7%
Neck	10	3.0%
Trunk	63	18.8%
Chest	39	11.6%
Diaphragm	1	0.3%
Abdomen	12	3.6%
Back	11	3.3%
Upper extremity	87	26.0%
Shoulder	9	2.7%
Arm	30	9.0%
Forearm	38	11.3%
Hand	10	3.0%
Lower extremity	148	44.2%
Buttock	7	2.1%
Thigh	73	21.8%
Leg	60	17.9%
Foot	8	2.4%
Not stated	1	0.3%
Total	335	

* Cases are listed for site of most extensive involvement.

TABLE IV
NUMBER OF MUSCLES INVOLVED

Involvement of Muscles	No.	%
One muscle	221	66.0%
Two muscles	42	12.5%
Three muscles	12	3.6%
Four muscles	4	1.2%
Five muscles		0.3%
Group (not specified)	55	16.4%
Total	335	

Multiple Tumors
   In 3 cases 2 separate muscles
   In 2 cases 3 separate muscles

A deformity was present in 86 cases (26 per cent), represented by increased diameter of an involved limb in 16, increased length of the limb in three, contracture or atrophy in 25, pes equinus in 21, exophthalmos in two, and other deformities in 19.

Impairment of function was observed in 84 cases (25 per cent). In 32 limitation of motion, varying in degree from slight to total incapacity of the part, was noted, and limitation because of pain in an additional 20. Weakness of an involved extremity was reported in six, due to replacement of muscle tissue or the large size of the tumor mechanically preventing a group of muscles from contracting normally. In 26 a limp was present.

Exploratory puncture was performed in 39 cases, yielding blood in all but one, and is a valuable aid in establishing the correct diagnosis.

Roentgenologic studies were made in 30 per cent of the cases. The most important finding is the presence of phleboliths in areas of the body in which there are normally no large plexuses of veins, thus indicating an abnormal collection of vascular channels, usually a hemangioma. Phleboliths are characterized roentgenographically as densely calcified, round or slightly oval, smoothly outlined areas, usually multiple, often exhibiting concentric laminations. They were present in 49 cases and absent in 51. Calcified parasites may rarely be confused with phleboliths. Trichinosis parasites are too small to appear except in excised muscle specimens. Cysticerci may become calcified but are not as dense, lack lamination in structure, are rarely present in groups, and are finely granular. Lymph nodes, tubercles, infarcts, chronic abscesses, fibroids, dermoids, hydatid cysts, or arteries may become calcified but differ from phleboliths in size, shape, and distribution. Myositis ossificans is recognized by its irregular streaky distribution.

A soft-tissue mass was noted in eight cases, and calcification of part of the tumor also in eight. Changes noted in the adjacent bone were a periosteal reaction in six, hypertrophy in one, eburnation in one, atrophy in two, and pressure erosion in one.

Angiography frequently permits visualization roentgenographically of hemangiomas, particularly those of the venous type, and is of value in determining the size, extent, and relationship to surrounding large vessels. It has also been employed to evaluate the results of treatment by sclerosing agents or deep roentgenotherapy. Venography is applicable to those cases in which the angioma is so situated that a tourniquet can be placed proximally to prevent rapid dispersion into the general circulation. The radiopaque material may be injected into a nearby vein or into the tumor itself. Arteriography is applicable to the arterial or arteriovenous type.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The diagnosis of hemangioma of muscle is difficult mainly because of the comparative rarity of the lesion and the depth of the tumor. However, the diagnostic features enumerated in Table V should enable one to make the

correct diagnosis in most cases if the existence of the lesion is kept in mind. Angiography is being employed with greater frequency and with increasing success as an adjunct in diagnosis.

TABLE V

INCIDENCE OF THE VARIOUS SALIENT DIAGNOSTIC FEATURES

Diagnostic Features	Present		Absent		Not Stated	
	No.	%	No.	%	No.	%
1. Age within first three decades....	241	72%	44	13%	50	15%
2. History of trauma.................................	57	17%	31	9%	247	74%
3. Mass or enlargement...............................	329	98%	6	2%	..:	....
4. Pain..........................:	200	60%	47	14%	88	26%
5. Deformity...	86	26%	31	9%	218	65%
6. Functional impairment.............................	84	25%	35	11%	216	64%
7. Blood on aspiration of tumor.......................	38	11%	1	0.3%	296	88%
8. Phleboliths on roentgen ray.......................	⌊49⌋	15%	51	15%	235	70%

The diagnosis was correctly made in 19 per cent of the cases and mentioned as an alternative diagnostic possibility in an additional 3 per cent (Table VI). Among the miscellaneous incorrect and alternative diagnoses not mentioned in the table were acute abscess, arthritis, synovitis, bursitis, myositis, myositis ossificans, osteomyelitis, phlebitis, pelvic cellulitis, syphilis (gumma and tenosynovitis), tuberculosis (of muscle, lymph, nodes, or bone), hematoma, varix, arteriovenous aneurysm, clubfoot, foreign body, hernia (epigastric, paraumbilical, and pulmonic), pseudo-elephantiasis, ossifying tumor, ganglion, bone tumor, hygroma, and malignant neoplasm.

TABLE VI

DIAGNOSES MOST COMMONLY MADE

Preoperative Diagnosis in 335 Cases

Preoperative Diagnosis	Definite		Alternative	
	No.	%	No.	%
1. Angioma..	65	19.4%	11	3:3%
Angioma of muscle..............................	35	10.4%	4	1:2%
Angioma (tissue not stated)......................	24	7.2%	7	2.1%
Angiofibroma....................................	1	0.3%	..	:....
Angiolipoma.....................................	1	0.3%	..	.....
Angiolymphoma..................................	4	1.2%	..	.....
2. Miscellaneous incorrect diagnoses......................	37	11.0%	12	3.6%
3. Lipoma...	19	5.7%	4	1.2%
4. Cyst (including dermoid)............................	10	3.0%	6	1.8%
5. Fibroma, neurofibroma, neuroma......................	10	3.0%	1	0.3%
6. Sarcoma...	8	2.4%	6	1.8%
7. Abscess (chronic)..................................	6	1.8%	3	0.9%
8. Aneurysm..	5	1.5%	1	0.3%
9. Benign neoplasm...................................	4	1.2%	2	0.6%
10. Myoma...	3	0.9%	1	0.3%
Diagnoses made (correct or incorrect)..............	167	49.9%	47	14.0%
None stated.....................................	168	50.1%		
Total cases..................................	335			

The clinical differentiation of hemangiomas of muscle from other benign neoplasms is not always easy, and in the case of small growths it may be necessary to examine the specimen microscopically before a final diagnosis can be made. Among this group a hemangioma is most frequently mistaken

TABLE VII

PATHOLOGIC, CLINICAL, AND LABORATORY FEATURES IN THE DIFFERENTIAL DIAGNOSIS OF HEMANGIOMAS OF STRIATED MUSCLE AND ANEURYSMS

Features	Hemangioma (Capillary, Cavernous, Venous)	Cirsoid Aneurysm (Arterial Hemangioma)	Arteriovenous Aneurysm	Simple Aneurysm
Pathologic				
Origin (Etiology)	Neoplastic	Controversial Neoplastic, congenital, traumatic	Congenital or traumatic	Infectious (luetic), degenerative, traumatic
Types	Capillary, cavernous, venous (Usually mixed)	Arterial hemangioma	Aneurysmal varix Varicose aneurysm	Fusiform Saccular
Communications	With vessels of similar type	Multiple A-V communications, usually of similar vessels	A-V communication, usually single, involving the larger peripheral vessels	With other arteries
Sac	None	None	Absent in aneurysmal varix Present in varicose aneurysm	Present
Clinical				
Characteristic age-group	First three decades, 85%	Young adult life	Any age	Middle age or later
Common location	Lower extremity 44%, Upper extremity 26%, Trunk 19%, Head 8%, Neck 3%	Scalp, face, hands, feet	Scarpa's triangle, popliteal space, axilla, cubital space, neck	Aorta Large peripheral vessels
Rapidity of enlargement	Slowly	Slowly. Sometimes rapidly, following trauma	Varies	Slowly
Pulsation	Absent, except in 2.1% Expansile in 1.2%	Usually present and expansile	Usually present and expansile	Usually present and expansile
Thrill	Absent, except in 0.6%	Often present, continuous type	Usually present, continuous type (most distinct over communication)	Usually present, interrupted type
Murmur	Absent except in 1.8%	Often present, continuous type	Usually present, continuous type	Usually present, interrupted type
Surface temperature of overlying skin	Usually normal	Usually increased	Usually increased in vicinity of aneurysm, but decreased distally	Usually normal
Veins of overlying skin	Usually normal Dilated in 3%	Usually prominent May pulsate	Usually prominent Usually pulsate	Usually normal
Arterial pulsation distal to lesion	Normal	Sometimes diminished	Usually diminished	Usually diminished

Pulse rate	Normal	Normal	Often mild tachycardia	Normal
Corrigan and capillary pulse	Absent	Absent	Sometimes present	Present only when ascending aorta is involved
Heart murmur (Transmitted from site of lesion)	Absent	Rarely present	Often present (Makin's murmur)	Sometimes present
Special clinical tests				
Branham's test (Compression of artery proximal to mass)	Negative	Rarely positive	Often positive (Bradycardia and rise in B.P.)	Negative. Almost complete disappearance of mass in extremity
Application of venous tourniquet distal to lesion	Filling may be prevented, and mass made less prominent	Filling not prevented, and mass made more prominent	No appreciable change	No change
B.P. below site of lesion	Normal	Usually normal	Usually decreased	Usually decreased
Secondary changes				
Collateral circulation	*Sometimes moderately increased	Moderately increased	Markedly increased	Moderately increased
Cardiac hypertrophy	None	Rarely	Usually	None, unless involves ascending aorta
Effect on growing extremity (Before closure of epiphyseal lines)	Length sometimes increased	Length sometimes increased	Length often increased	Indeterminate
Edema of an extremity	Usually absent	Sometimes present	Frequently present	Sometimes present
Complications	Deformity 26% Functional impairment 25%	Ulceration (rarely) Hemorrhage (rarely)	Terminal atrophy; trophic ulcers, elephantiasis, gangrene	Ulceration (not uncommon) Rupture (not uncommon)
Laboratory				
Wassermann and Kahn tests	Negative	Negative	Negative	Often positive
Oxygen content of venous blood from lesion	Normal	Increased	Approaches that of arterial blood	Normal
Phleboliths on roentgen ray	Present in 49%	Rarely present	Absent	Absent
Angiography	Mass may be outlined by venography	Extent may be visualized both by arteriography and venography	Fistula may be visualized both by arteriography and venography	May be visualized by arteriography

* Markedly increased in author's case 1.

for a lipoma because of its lobulation, softness, and compressibility. Changes in size and consistency with change of posture, and aspiration of blood on exploratory puncture should rule out lipoma. Fibromas and neurofibromas as a rule are very firm, usually sharply demarcated from the surrounding tissues, and grow more rapidly than hemangiomas. A hemangioma with a dense fibrous tissue stroma would be difficult to distinguish clinically from these tumors, but aspiration of blood from the tumor should again be of aid in differentiation.

Because of its smooth contour and occasional pseudofluctuation, a hemangioma of muscle may resemble a cyst. Careful examination will usually reveal that the mass is in the muscle, thus eliminating dermoid cysts which are not found in the voluntary muscles of the extremities. Hydatid cysts yield yellow fluid on puncture, rather than blood, in which characteristic hooklets may be found. The Casoni intradermal reaction which is both rapid and specific for echinococcosis may also be employed.

Primary sarcoma of the muscle itself is exceptionally rare, but sarcoma arising in the intermuscular connective tissue represents a definite diagnostic possibility. As a rule these tumors are fairly rapid in growth and prone to metastasize. The patient may show some of the systemic manifestations of malignancy, whereas the patient with a hemangioma is practically always in good general health. Myoblastomas and rhabdomyomas are usually malignant, extremely rare, and as a rule occur in tissues other than voluntary muscle.

Hemangiomas of muscle have been confused with a large variety of inflammatory lesions, as already enumerated. The onset clinically, often following trauma, with the accompaniment of pain and local tenderness, accounts for the relative frequency with which such diagnoses are made. Indeed, it is entirely possible for a hemangioma to become inflamed following trauma, and histologic evidence of this was noted in several of the specimens removed at operation. In most cases, however, the absence of fever and leukocytosis militates against the diagnosis of an inflammatory lesion. Serologic tests should rule out syphilis. In cold abscess or tuberculous myositis an exploratory puncture may show thin serous fluid with caseous detritus. In nonspecific chronic myositis there is a history of repeated trauma followed by the appearance of an extremely firm, hard mass. Myositis ossificans may be diagnosed by roentgenography which demonstrates bone formation within the muscle.

In hematomas aspirated blood is not normal as in hemangiomas, but is dark if removed early and is serum if removed later. Furthermore, the mass remains smaller following aspiration, whereas a hemangioma again resumes its previous size.

Finally, in the unusual instances in which the tumor pulsates and a bruit is heard, as for example in the authors' first case, the diagnostic possibility of aneurysm must be entertained. The salient features in the differential diagnosis of hemangiomas and aneurysms are summarized in Table VII, including percentages of exceptions whenever possible.

Table VIII

VARIOUS TYPES OF TREATMENT AND RESPECTIVE END-RESULTS

TREATMENT AND RESULTS

TREATMENT	No.	%	RESULTS							
			IMPROVEMENT OR CURE No.	%	RECURRENCE OR NO IMPROVEMENT No.	%	DEATH No.	%	NO STATEMENT No.	%
I LOCAL EXCISION	265	79.1%	240	90.6%	13	4.9%	-	-	12	4.5%
II PARTIAL EXCISION	17	5.1%	11	64.7%	3 [a]	17.6%	-	-	3	17.6%
III AMPUTATION	4	1.2%	2	50.0%	1	25.0%	-	-	1	25.0%
IV INJECTION OF SCLEROSING SOLUTION	3	0.9%	3	100%	-	-	-	-	-	-
V X-RAY THERAPY	2	0.6%	2 [b]	100%	-	-	-	-	-	-
VI MISCELLANEOUS	44	13.1%	11	25.0%	3	6.8%	1	2.3%	29	65.9%
A EXCISION FOLLOWED BY ROENTGEN THERAPY	5	1.5%	3	60.0%	1	20.0%	-	-	1	20.0%
B PARTIAL EXCISION FOLLOWED BY RADIUM THERAPY	1	0.3%	-	-	1	100%	-	-	-	-
C PARTIAL EXCISION FOLLOWED BY ELECTROCOAGULATION	1	0.3%	1	100%	-	-	-	-	-	-
D PARTIAL EXCISION FOLLOWED BY INJECTION OF SCLEROSING SOLUTION	1	0.3%	1	100%	-	-	-	-	-	-
E RADIUM THERAPY FOLLOWED BY EXCISION	1	0.3%	-	-	1	100%	-	-	-	-
F EXCISION AND ACHILLES TENOTOMY	2	0.6%	2	100%	-	-	-	-	-	-
G ACHILLES TENOTOMY	2	0.6%	2	100%	-	-	-	-	-	-
H CAUTERIZATION (GALVANIC)	1	0.3%	1	100%	-	-	-	-	-	-
I TREATMENT NOT STATED OR NONE GIVEN	30	9.0%	1	3.3%	-	-	1 [c]	3.3%	28	9.3%
TOTAL	335		269	80.3%	20	6.0%	1	0.3%	45	13.4%

(a) In case 1 of Riethus amputation was performed 8 months later.
In case 4 of Furlkroger a Pirogoff amputation was subsequently performed.
(b) In case 4 of Fulton and Sosman there was previous exploratory inclusion and biopsy.
(c) Death of a premature infant one half hour after delivery.

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TREATMENT AND RESULTS

The various types of treatment employed and the respective end-results are summarized in Table VIII.

I. In 265 cases (79 per cent) the tumor was locally excised, with improvement or cure in 90 per cent. The ideal in treatment is to effect complete surgical excision well beyond the confines of the tumor before excessive growth and irreparable deformity have occurred, to achieve good hemostasis, and to preserve or restore normal function of the part. General anesthesia is the one of choice in most instances. Surgical extirpation is comparatively easy only in the circumscribed type, in which the tumor may often be removed by simple enucleation. In the partially circumscribed or diffuse types, excision is attended with much greater technical difficulties, since it is desirable to resect muscle tissue well beyond the limits of the tumor and since important contiguous large vessels or nerves are apt to be injured. In at least 40 cases, including the authors' first case, the problem of control of hemorrhage was a major issue of the operation, and in several cases large hematomas developed postoperatively. The employment of measures to obtain as nearly a bloodless field as possible is advocated both to prevent hemorrhage and to permit visualization of all parts of the tumor. This may be accomplished by the use of a tourniquet (authors' Case 2), Esmarch bandage (Montant; Sorensen, Case 1; Huet, Case 2), or ligation of large vessels of supply to the tumor either permanent (Owen; Luz, Case 1), or temporary (authors' Case 1). Recurrence or no improvement occurred in 13 cases (5 per cent). Further surgery may thus be required secondarily to remove remnants missed at operation or to correct deformities following necessarily wide removal.

II. Partial excision was performed in 17 cases (5 per cent), with improvement resulting in 65 per cent. It was employed in cases in which complete removal was impossible without damaging large nerves or blood vessels, or in which hemorrhage became so marked that the operation had to be terminated (case of McNealy). Partial excision alone was associated with recurrence or lack of improvement in 18 per cent of the cases in which it was employed. It was sometimes followed by other types of treatment as roentgenotherapy (Thomas, Case 1), radium therapy (Davis and Kitlowski, Case 7), sclerosing solution (Pomeranz and Tunick, Case 4), and electrocoagulation (Cascio), usually with improvement. In Furlkroger's case and Case 1 of Riethus amputation was subsequently required.

III. Amputation is reserved for those cases in which previous attempts at excision have failed (Furlkroger, Riethus), or in which the tumor is so extensive and deformity so marked that simple removal would not suffice (Nast-Kolb; Verebely; Mauro, Case 1; Davis and Kitlowski, Case 2).

IV. Pomeranz and Tunick advocate the use of sclerosing agents, stating that such a measure avoids open operation and may afford satisfactory relief. Kidner states that small hemangiomas of muscle may be treated in this manner with success, but that in large ones it is difficult to reach all parts of the tumor and there is danger of producing necrosis. Peyton and Leven,

in a limited experience, claim satisfactory results with this method. The material is injected at intervals of from one to several weeks, depending on the amount of reaction produced, preferably into, but permissibly about, the vessels of the angioma, applying proximal pressure to lessen the tendency of the sclerosing agent to diffuse beyond the angioma.

Other authors, such as Watson and McCarthy, commenting on a series of over 1,000 hemangiomas in general, including ten of skeletal muscle, do not recommend this form of treatment, stating that the fast flowing blood stream sweeps the solution out of the large sinuses before sclerosis or thrombosis can be effected, and that even when compression is maintained during and immediately after injection the results are not satisfactory.

. The very few reports in the literature are not sufficient to warrant definite conclusions as to the value of the method. It seems that at best, however, this type of treatment is a palliative one, relieving symptoms or reducing the size of the tumor without effecting a definite cure. Its ultimate value may be in its judicious combination with other methods of treatment such as partial excision or roentgenotherapy in those very widespread cases in which only amputation would seem to suffice.

V. According to Watson and McCarthy, high voltage roentgen ray may be used in the treatment of inoperable extensive muscle angiomas. These authors have observed that the radiosensitivity varies in inverse proportion with the age of the patient, responding best in infants under three months and less after six months of age. Clinical experience indicates, however, that these angiomas do not respond as well to irradiation as those of the skin and brain. Deep roentgenotherapy alone was used in the treatment of venous hemangiomas of muscle, followed by relief of pain and decrease in the size of the intercommunicating vessels, in Cases 1 and 4 of Fulton and Sosman. The decrease in the size of the vessels was demonstrated by the comparison of venograms, thus rendering it difficult to be certain that the decrease was due to the roentgenotherapy alone, since the radiopaque solution used to outline the angioma in itself acts as a mild sclerosing agent, and, indeed, was used by Pomeranz and Tunick as a form of treatment.

In addition to its possible value in very extensive cases in which complete removal is impossible, roentgen ray radiation may also be indicated post-operatively in those cases in which the histologic picture of the tumor is more cellular than usual (authors' Case 1), or in which there is a suspicion of malignant degeneration (case of Teller, Solis-Cohen, and Levine). In such cases local recurrence or even metastasis may possibly be prevented or delayed.

VI. Miscellaneous forms of treatment accounted for 13 per cent of the cases. Some of the combinations listed in Table VIII have already been discussed. Radium therapy was employed once prior to excision (Thomas, Case 2), and once following partial excision (Davis and Kitlowski, Case 7), with an unsatisfactory outcome in both instances. Cauterization with galvanic current, followed by cure after several months of treatment, was reported by Wharton. Achilles tenotomy, aimed only at correction of the orthopedic

TABLE IX

CASES OF HEMANGIOMATOUS TUMORS OF SKELETAL MUSCLE

Supplementing the Table of Davis and Kitlowski and Extended by Jenkins and Delaney

No.	Author	Age Sex	History	Findings Muscle Involved	Preoper. Diag. Treatment Result	Pathologic Type
1	Bartoli	24 M	Painless tumor for indefinite period	Walnut-sized tumor.	Excision. Recovery	Cavernous hemangioma
2	Biasini	22 M	Slowly growing tumor since age 1.	Tongue and sternocleidomastoid. Soft, reducible, nontender tumor. Sternocleidomastoid	Angiocavernoma. Excision. Recovery	Angiocavernoma
3	Bishop	19 M	Recurred following removal at age 5. Swelling of leg for two years and slight limp	Orange-sized, freely movable swelling of posterior surface of leg. Atrophic calf muscles. Pressure erosion of fibula and calcification in soft tissues on roentgen ray. Probably peroneus longus	Partial excision	Diffuse hemangioma. Small islets of heterotopic bone in stroma
4	Bocchi (Faldini)	8 F	Tumor of anterior lower third of arm following trauma two years previously	Almond-sized, tender mass. Forearm held preferably in flexion. Eburnation of cortex of humerus on roentgen ray. Brachialis	Inflammatory lesion of humerus. Excision. Recovery	Diffuse hemangioendothelioma
5	Bouquet and Beaujeu	? M	Painful area on forearm for two years	Forearm diffusely swollen, soft, and fluctuant. Multiple angioliths on roentgen ray. Muscles of forearm	Hemangioma. Excision and deep roentgen ray therapy. Recovery	Infiltrating cavernous hemangioma
6	Cace	13 F	Right leg slightly larger than left since birth and painful on exertion	Pes equinovarus. Periosteal reaction and curving of fibula on roentgen ray. Gastrocnemius	Excision	Diffuse angioma fibrosa
7	Cace	35 F	Enlarging tumor of posterior aspect of elbow since adolescence	Hen's egg-sized, soft, irreducible tumor. Overlying skin bluish. Limitation of flexion. roentgen ray neg. Triceps brachii	Excision	Circumscribed angiomatous tumor
8	Calka	39 M	Enlarging swelling of upper part of forearm for ten years, following trauma	Fist-sized swelling containing a pea-sized painful lump. Multiple phleboliths on roentgen ray. Muscles of forearm	Hemangioma	
9	Carnevali	13 F	Painful knee and thigh for six years	Painful, firm swelling of thigh posteriorly. No angioliths on roentgen ray. Biceps femoris	Excision. Recovery	Diffuse cavernous hemangioma
10	Carnevali	17 M	Left lower extremity underdeveloped and painful for two years	Tender, hazel nut-sized tumor on medial aspect of thigh. Roentgen ray neg. Vastus medialis	Excision. Recovery	Circumscribed cavernous hemangioma

TABLE IX (*continued*)

No.	Author	Age/Sex	History	Clinical findings	Treatment and outcome	Diagnosis
11	Carnevali	7 F	Painful calf for one year	Involved leg slightly underdeveloped. Pes equinus. Roentgen ray neg. Muscles of calf	Biopsy. Subsequent excision and achillo tenotomy. Recovery	Diffuse cavernous hemangioma
12	Carnevali	2 F	Painful, swollen plantar surface of foot for six months	Soft, tender tumor on medial border of foot. Short plantar muscles	Excision. Recovery	Diffuse cavernous hemangioma
13	Carnevali	6 F	Pain in leg for two years and swelling of calf for one year	Tender, walnut-sized tumor of calf. Gastrocnemius	Excision. Recovery	Diffuse cavernous hemangioma
14	Doederlein	New born M	Death 30 min. after premature delivery	Origin in right half of diaphragm with extension to serratus ant., intercostal muscles, and soft tissues of chest and abdominal walls. Hypoplasia of rt. lung and bilateral hydrothorax	Death	Diffuse capillary hemangioma
15	Falcao	23 F	Tumor of side of face for five years	Soft mass, enlarging on obstructing return blood flow. Masseter	Angioma	
16	Forty (Leather)	20 F	Painful swelling of dorsum of foot for 13 mos.	Soft, compressible tumor. Expansile pulsation, abolished by compressing dorsalis pedis. Roentgen ray neg.	Excision	Diffuse hemangioma
17	Freeman	10 F	Painful tumor of thigh for past five mos., following trauma one year previously	Almond-sized, compressible tumor of lateral surface of thigh. Roentgen ray neg. Vastus lateralis	Sarcoma. Excision. Suggestion of recurrence four mos. later	Nonencapsulated cavernous hemangioma
18	Fulton and Sosman (Case 1)	23 F	Recurring pain and swelling of arm for 13 years	Swelling over elbow and pain on extension beyond 160°. Phleboliths on roentgen ray. Large venous lacunae visualized by venography. Muscles of arm	Venous angioma of muscle. Roentgen ray therapy. Relief of pain	Cavernous hemangioma
19	Fulton and Sosman (Case 2)	32 F	Persistent swelling and pain following removal of tumor of elbow 16 years previously	Soft, tender mass containing a hard nodule. Soft tissue shadow with phleboliths on roentgen ray. Triceps brachii	Venous angioma of muscle. Excision. Well 2.5 years later	
20	Fulton and Sosman (Case 4)	20 M	Painful foot for four years	Tender swelling of sole. Plantar flexion of toes limited. Phleboliths on roentgen ray. Plantar muscles (second layer)	Venous angioma of muscle. Biopsy and roentgen ray therapy. Relief of most of pain	
21	Gaudier	9 F	Enlarging tumor of thigh for one year	Soft, nontender tumor on lateral aspect of thigh. Blood on aspiration. Vastus externus	Angioma of muscle. Esmarch bandage and excision. No loss of function	Diffuse hemangioma
22	Huard, Joyeux, and Vu Thanh	11 M	Painful forearm for 1.5 years	Diffuse, soft, nontender tumor of ant. aspect of forearm. Grasp weak. Angioliths on roentgen ray. Flexor muscles of forearm.	Excision. Good functional result	Diffuse hemangioma

TABLE IX (*continued*)

No.	Author	Age Sex	History	Findings Muscle Involved	Preoper. Diag. Treatment Result	Pathologic Type
23	Huet	22 M	Tumor of forearm for five years, with pain and paresthesias for two years. Surgical exploration one year previously	Walnut-sized, soft, nontender tumor or ant. aspect of forearm. Calcified nodules on roentgen ray. Muscles of forearm	Angioma of muscle. Excision. Pulmonary tuberculosis six mos. later	Diffuse capillary angioma
24	Huet	25 M	Painful tumor of sole excised 15 years previously, but recurred	Firm, tender, turkey's egg-sized tumor, with ulceration of sole. Angioliths on roentgen ray. Plantar muscles	Angioma of plantar muscles. Esmarch bandage and excision. Complete recovery	Angioma
25	Imperati	13 M	Painful calf for four years	Oval tumor of calf. Blood on aspiration. Roentgen ray neg. Gastrocnemius	Angioma. Biopsy	Diffuse cavernous hemangioma
26	Josefsson (V. Rosen)	12 F	Painful, swollen calf for past six years	Tender mass in calf. Pes equinus and atrophy of leg. Roentgen ray neg. Soleus	Excision. Achillotenotomy two weeks later. Good correction of deformity	Diffuse cavernous hemangioma
27	Kidner	24 F	Persistent tenderness of calf following excision of tumor associated with trauma	Compressible mass of calf seven inches long. Gastrocnemius and soleus	Angioma. Excision followed by two subsequent excisions within six mos. No recurrence in 15 years	Diffuse cavernous hemangioma
28	Kidner	10 F	Pain in leg, and limp for four years. Lump in calf for one year	Tender tumor of calf. Congenital malformation of tarsus. Gastrocnemius and soleus	Excision and roentgenray therapy. Bruit developed probably due to A-V connection	Diffuse cavernous and telangiectatic hemangioma
29	Kidner	39 M	Painful swelling of calf for seven years	Soft tumor of calf. Few varicose veins. Gastrocnemius and soleus	Cavernous angioma. Excision. Relief of pain	Grossly, a diffuse cavernous hemangioma
30	Kidner	8 M	Swelling of leg and limp for three years. Severe pain on one occasion	Soft, tender swelling lateral to Achilles tendon. Hypertrophy of tibia on roentgen ray. Gastrocnemius; soleus, peronei	Cavernous angioma. Incomplete excision. Relief of pain	Diffuse cavernous hemangioma
31	Kriener	58 M	Incidental discovery	Increase in circumference of forearm five cm. Nodules palpable. Swelling disappears on elevation. Phleboliths on roentgen ray. Muscles of forearm	Cavernous hemangioma of muscle. Biopsy	Diffuse cavernous hemangioma

TABLE IX (continued)

No.	Author	Age/Sex	History	Physical findings	Diagnosis and treatment	Pathologic diagnosis
32	Luz	20 M	Enlarging mass on buttock for three years	Compressible fluctuant mass with pulsation and systolic bruit. Gluteus maximus	Gluteal aneurysm. Ligation of hypogastric artery and partial excision. Recovery	Diffuse hemangioma
33	Luz	47 M	Slowly growing tumor on thoracic area of back	Firm, compressible, nontender tumor. Trapezius	Lipoma. Excision. Recovery	Diffuse hemangioma
34	MacDermott	24 F	Pain and swelling of calf for seven years	Calf enlarged. Roentgen ray neg. Gastrocnemius and soleus	Pseudo-elephantiasis or angioma. Excision. No recurrence in two years	Partially circumscribed angioma
35	MacDermott	12 M	Swelling to right of middorsal region for three years	Resilient, duck's egg-sized mass. Blood on aspiration. Erector spinae	Hemangioma, sarcoma; spinal caries; hernia pulmonis. Excision. Well after two years	Partially circumscribed fibrohemangioma
36	Mailer	21 M	Enlarging mass in arm following trauma four months previously	Tender, hen's egg-sized mass on inner posterior aspect of arm. Triceps brachii	Fibroma of triceps. Excision. Recovery	Diffuse capillary and arterial angioma
37	Maure	8 F	Pain and paresthesia of forearm and hand for two years	Palmar and forearm swelling, increasing with obstruction of venous return. Volar muscles of forearm	Hemangioma. Amputation of lower third of arm	Diffuse cavernous hemangioma
38	Mauro	40 F	Painful swelling of interscapular area for one year	Lemon-sized, soft tumor. Rhomboidei	Excision and further excision two mos. later. No recurrence in four years	Encapsulated cavernous hemangioma, with sarcomatous degeneration
39	McNealy	28 M	Tumor of popliteal space for several years. Attempted excision nine months previously	Tumor mass of popliteal space. Semimembranosus	Excision. Probable cure	Hemangioma
40	Mondolfo	12 M	Painful calf and pes equinus for two years	Hard, tender, pigeon's egg-sized tumor of calf. Leg underdeveloped. Roentgen ray neg. Gastrocnemius	Angioma. Excision and application of apparatus to correct pes equinus. Fair correction	Circumscribed angioma musculare
41	Mondolfo	9 F	Increasing swelling of calf since birth. Pain in leg for past five years	Enlargement and soft consistency of calf. Several small hard nodules. Slight pes equinus. Irregular soft tissue shadows on roentgen ray. Muscles of calf	Angioma. Two excisions six mos. apart. Partial correction of pes equinus	Diffuse angioma musculare
42	Mondolfo	21 F	Enlarging of lower extremity, contracture of knee, and pes equinus since age of 14	Muscles firm and elastic. Flexion contracture of knee and pes equinus. Irregular soft tissue shadows on roentgen ray. Muscles of lower extremity	Diffuse angioma, primary in muscles. Amputation refused	Diffuse angioma musculare

TABLE IX (continued)

No.	Author	Age Sex	History	Findings Muscle Involved	Preoper. Diag. Treatment Result	Pathologic Type
43	Mondolfo	10 F	Painful swollen calf with increasing pes equinus since birth	Soft, tender swelling of calf and marked pes equinus. Irregular soft tissue shadow on roentgen ray. Muscles of calf	Angioma of muscles. Achillotenotomy. Partial correction six months later	Diffuse cavernous hemangioma
44	Montant	23 M	Trauma to forearm four years previously, followed by gradually increasing pain and swelling	Decrease in size on elevation. Pain on moving fingers. Periosteal reaction on roentgen ray. Arteriography neg. Volar muscles of forearm	Syphilitic tenosynovitis. Esmarch bandage and excision. Relief of pain; normal function	
45	Nicolosi	7 F	Enlarging painful swelling posteriorly on thigh for three years	Soft, tender, egg-sized tumor, increasing in size when patient stands. Biceps femoris	Hemangioma of muscle. Excision. Recovery	Partially circumscribed cavernous hemangioma
46	Nicolosi	9 M	Enlarging painless tumor of forearm for one year	Elastic, ill-defined, egg-sized tumor, decreasing on elevation of arm. Limitation of pronation. Volar muscles of forearm	Hemangioma of muscles. Excision. Recovery	Diffuse cavernous hemangioma
47	Oi and Yazaki	16 M	Painful swelling of knee and buttock since childhood	Tumor above lateral aspect of knee, on lateral aspect of thigh, and on buttock. Flexion of knee limited. Blood on aspiration of knee and buttock tumors. Phleboliths on roentgen ray. Biceps femoris; vastus lateralis; gluteus maximus	Multiple primary muscle angiomas. Excision. Recovery	Diffuse cavernous hemangioma
48	Owen	24 F	Enlarging painful tumor of side of face since age of seven. Attempted operation and roentgen ray therapy at age of 19	Lemon-sized, compressible, expansile, pulsating tumor. Roentgen ray neg. Muscles of jaw	Ligation of external maxillary vessels. Excision. Well 33 months later	Diffuse hemangioma
49	Pomeranz and Tunick	5 M	Tumor of sole since birth. Ulceration and pain following roentgen ray and radium therapy	Pes equinovarus. Atrophy of foot and calf. Ulcer on plantar surface and edema of dorsum. Nodular soft tissue mass and phleboliths on roentgen ray. Venogram showed dilated vessels. Muscles of foot	Angioma. Injection of sclerosing agents. Ulcer healed in six weeks. Contour of foot still normal three years later	
50	Pomeranz and Tunick	3 M	Painful swellings of forearm and hand since birth	Flat, tender, fluctuating masses on dorsum of forearm. Veins of palm dilated. Phleboliths on roentgen ray. Venogram outlined clumps of vessels. Muscles of forearm.	Injection of sclerosing agents. Tumor obliterated and pain gone three weeks later	

Muscles of forearm.

TABLE IX (continued)

No.	Author	Age/Sex	History	Physical findings	Treatment and result	Diagnosis
51	Pomeranz and Tunick	3 F	Slowly growing painful tumor of leg since birth	Hard, irregular swelling on ant. surface of leg. Two tender masses behind external malleolus. Swelling of dorsum of foot. Phleboliths on roentgen ray. Muscles of leg	Syphilis? Muscle angioma? Injection of 20 cc. of hippuran. Excellent result six months later	Diffuse angiomatosis (biopsy report)
52	Pomeranz and Tunick	17 M	Injured elbow 14 years previously. Four months later developed an enlarging soft tissue swelling	Lobulated, semi-elastic mass on elbow. Pressure caused ulnar nerve pain. Phleboliths on roentgen ray. Muscles of forearm	Partial excision and sclerosis. Mass reduced, pain gone, and vessels obliterated one year later	
53	Poos	43 M	Increasing exophthalmos of right eye for five years	Exophthalmos and limitation of motion. Elastic, tense tumor on temporal side. Roentgen ray neg. Muscles of cone of orbit	Retrobulbar cyst. Krönlein operation and excision	Circumscribed hemiangioma cavernosum
54	Poos	12 F	Increasing exophthalmos of left eye for two years	Exophthalmos increases on bending. Limitation of motion. Clouding of orbit on roentgen ray. Muscles of cone of orbit	Krönlein operation and excision. Return of function	Circumscribed cavernous hemangioma
55	Picardi (Chiasserini)	35 F	Increasing swelling of arm for ten years. Paresthesias of ulnar nerve following unsuccessful surgical intervention	Lemon-sized, elastic tumor, with pulsation and continuous fremitus and murmur accentuated in systole. Biceps brachii	Excision. Recovery	Diffuse angioma-arterioso
56	Ricci	8 F	Swelling of calf since age 1, and pain since age 4	Tender swelling of calf. Gastrocnemius and soleus	Excision. Recovery	Diffuse cavernous hemangioma
57	Rocher and Roudil	9 M	Enlarging painful tumor following fall on elbow	Soft, tender almond-sized tumor. Radial muscles of forearm	Synovial cyst. Excision. Recovery	Circumscribed angiofibroma
58	Rocher and Uzac	46 F	Enlarging tumor of forearm since youth	Soft, lemon-sized tumor. Volar muscles of forearm	Angioma. Excision. Good function	Diffuse capillary hemangioma containing a small osteoma
59	Serra, Lavenia, and Frega (Sussini)	24 F	Painful swelling of lateral chest wall for one year	Soft, partially reducible tumor, 3 x 12 cm. Pulsation, with thrill and continuous murmur. Muscles of right hemithorax	Excision. Recovery	Arteriovenous angioma
60	Settergren	21 M	Painful thigh, following trauma five years previously	Tenderness and suggestion of mass in thigh. Roentgen ray neg. Vastus musculature	Hemangioma of vastus. Esmarch bandage and Excision.	Circumscribed cavernous hemangioma
61	Settergren	27 M	Painful swelling of arm following trauma two months previously. Similar swelling excised 23 years previously	Swelling slightly larger than hen's egg. Bicep's brachii	Well three years later Symptom-free four years later	Diffuse cavernous hemangioma

TABLE IX (*continued*)

No.	Author	Age Sex	History	Findings Muscle Involved	Preoper. Diag. Treatment Result	Pathologic Type
62	Settergren	57 F	Chest trauma 29 years previously, followed by a lump and aching pain	Firm, slightly movable, walnut-sized tumor. Musculature at tip of twelfth rib	Excision	Cavernous hemangioma
63	Soli	7 M	Tumor of neck discovered by a barber two years previously	Firm, reducible, nontender, walnut-sized tumor. Splenius capitis	Hemangioma of muscle. Excision. Recovery	Circumscribed cavernous hemangioma
64	Sorensen	47 F	Painful swelling of dorsum of hand for one year	Soft, noncompressible tumor on fourth metacarpal interspace. Atrophy and deformity of fourth and fifth metacarpals on roentgen ray. Interossei	Lipoma; Rhabdomyoma; sarcoma. Esmarch bandage and excision. Well three years later	Hemangiofibroma cavernosum
65	Sorensen	25 F	Painful nodule in first metacarpal space for one year	Tender, freely movable, pea-sized nodule. Phleboliths on roentgen ray. Adductor pollicis	Hemangioma of muscle. Excision. Well three years later	Circumscribed hemangiofibroma
66	Sorensen	15 F	Nodule of second metacarpal interspace for two years, painful for six months	Tender, walnut-sized mass. Roentgen ray neg. Interossei	Hemangioma of muscle. Excision. Well one year later	Circumscribed hemangiofibroma cavernosum
67	Stewart	8 M	Nodule of thigh for one year	Hard nodule on external surface. Vastus lateralis	Sarcoma. Excision	Hemangioma
68	Talbot and du Bourguet	? M	Pain in lower thigh on exertion	Tender, fluctuant, egg-sized mass. Size varies with position of limb. Blood on aspiration. Roentgen ray neg. Vastus internus	Vascular tumor of muscle. Excision. Recovery	Angiolipoma
69	Teller, Solis-Cohen, and Levine	63 F	Tumor of leg for 22 years, enlarging during the past ten years. Pain on walking	Large tumor mass of ant. aspect of leg. Periosteal proliferation of tibia and fibula on roentgen ray. Tibialis anterior	Periosteal fibroma or fibrosarcoma. Excision followed by roentgen ray therapy	Diffuse cavernous hemangioma
70	Thomas (Hedblom)	6 M	Tumor of chest since birth. Lymphangioma of inguinal region since birth and congenital malformation of feet	Painless, compressible chest tumor. Purplish discoloration of overlying skin. Blood on aspiration. Muscles of chest wall	Partial excision and roentgen ray therapy. Well two years later. Died four years after inguinal operation	Hemangioma with secondary inflammatory changes
71	Thomas	3 M	Swelling, blueness, and pain in knee for two years	Fluctuant swelling, size of half a lemon. Roentgen ray neg. Quadriceps femoris	Radium therapy and excision. Second operation one year later for recurrence. Improved five months later	Cavernous hemangioma
72	Thomas and Hark	15 F	Painful enlarging mass in calf for eight years, following trauma	Tender mass 10 x 20 cm., adherent to Achilles tendon. Gastrocnemius	Excision and later excision of tumor involving flexor hallucis longus. Primary healing	Diffuse cavernous hemangioma

TABLE IX (*continued*)

TABLE IX (continued)

	Author	Age/Sex	History	Physical findings	Treatment and outcome	Diagnosis
				ing flexor hallucis longus. Primary healing		
				Gastrocnemius		
73	Thomas and Hark	7 F	Painful knee and limp for nine months	Flexion contracture of knee. Popliteal space exquisitely tender. Calcareous shadows on roentgen ray. Semimembranosus	Angioma? Malignancy? Excision of two masses, and one involving posterior tibial nerve not removed	Cavernous hemangioma
74	Truesdell	30 F	Backache for five years	Slight prominence below twelfth rib posteriorly. Erector spinae	Exploratory operation and excision. Relief of symptoms	Hemangioma
75	Verebely	20 F	Enlarging painful swelling of calf for three years. Red birthmark of thigh removed eight years previously	Leg three times enlarged. Knee held at 45°. Pes equinus and edema of foot. Overlying skin hard. Flexor and peroneus muscles of leg	Sarcomatous tumor of muscle. Supracondylar amputation. Recovery	Extensive hemangiomatosis of muscle
76	Watson and McCarthy	14 F	Painful swelling of forearm for five years	Swelling 7 x 4 x 2 cm. Muscles of forearm	Excision. Recovery	Cavernous hemangioma
77	Weaver (Francisco)	10 F	Trauma five years previously, followed by a nodule which enlarged and became tender	Small, tender, compressible tumor of dorsum of foot. Extensor digitorum brevis	Excision and another for recurrence two years later. Well two years later	Cavernous hemangioma
78	Weaver	20 M	Pain and weakness of leg and tenderness of thigh following diphtheria eight years previously	Small, tender, nodule above lateral condyle of knee. Atrophy of thigh and calf. Roentgen ray neg. Vastus lateralis	Excision. Three years later symptom-free and both legs almost same size	Cavernous hemangioma
79	Weaver (Francisco)	13 F	Pain in knee for seven years. Limp and tenderness of knee for four	Atrophy of thigh and calf. Extension of knee limited to 160° and flexion to 85°. Phleboliths on roentgen ray. Vastus lateralis	Excision. Return of normal function	Obliterated hemangioma
80	Zappala	11 F	Swelling and pain in calf for four years	Tender, somewhat reducible, egg-sized tumor. Soft tissue shadow on roentgen ray. Gastrocnemius	Excision. Recovery	Diffuse cavernous fibro-angioma
81	Authors (Shallow)	35 F	Enlarging mass of thigh, following delivery five years previously. Pain on exertion	Smooth, difficultly compressible, nontender, slightly movable mass on thigh. Pulsation and bruit. Roentgen ray neg. Vastus lateralis; gluteus maximus; tensor fasciae latae	Angioma or aneurysm. Temporary ligation of common iliac artery. Excision and roentgen ray therapy. Normal function preserved	Partially circumscribed hemangio-endothelioma
82	Authors (Shallow)	10 M	Enlarging, painful lump following trauma six months previously	Soft, tender, walnut-sized mass. Systolic bruit. Roentgen ray neg. Triceps brachii	Hemangioma or aneurysm. Excision followed by recurrence two years later. Further excision. Normal function restored	Diffuse cavernous hemangioma

Note: Since completion of this article, two cases of hemangio-endothelioma of skeletal muscle have been reported by Stout and one case of venous hemangioma by Light.

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defect, was performed in two cases, followed by improvement. In 30 cases (9 per cent) the treatment was not stated or else no definitive treatment was given. In six of these only a biopsy was performed, and in two the tumor was merely exposed without being excised. In one case amputation was refused, and there is no report of the outcome.

In consideration of the various forms of treatment, it is evident that complete surgical excision offers the only hope of permanent cure. In late or very widespread cases such a procedure is often unfeasible, and a judicious combination of partial excision followed by deep roentgenotherapy or use of sclerosing agents may be employed.

PROGNOSIS

Complete recovery is the rule, and in spite of the frequent sacrifice of large amounts of muscle tissue the functional result is usually very satisfactory. In both of the authors' cases there was extensive removal of muscle, and yet in Case 1 normal function was preserved and in Case 2 restored. There was no surgical mortality for the entire series.*

Recurrence locally of the tumor or lack of improvement was reported in 6 per cent of the series, and postoperative deformity in 4 per cent. There was limitation of motion in three cases, a limp in one, persistence of limp in one, loss of function of a muscle in one, atrophy of muscle in one, persistence or occurrence of contracture in four, pes equinus deformity in one, and other deformities in two.

Although in several cases an increased cellularity of the tumor, histologically, was suggestive of malignancy, there are no recorded cases primary in muscle in which metastasis has occurred.*

The only death occurred in Doederlein's case of a premature infant one-half hour after delivery.*

SUMMARY AND CONCLUSIONS

An analytic review is made of 335 cases of primary hemangiomatous tumors of skeletal muscle. Included are two cases of our own, one most unusual and the other ordinary for comparison.

The disease occurs about equally in both sexes and most frequently (85 per cent) during the first three decades of life.

The prevailing view is that hemangiomas are congenital tumors, originating from abnormal embryonic sequestrations of vascular tissue. Trauma and systemic infection acting as secondary factors may in some instances modify subsequent growth and clinical manifestations.

The lesion arises in the vascular plexus of the muscle or in the perimysium between the muscle fibers, and grossly often resembles a muscle containing varicose veins. Diffuse, partially circumscribed, and circumscribed types are recognized. The diffuse type is by far the most frequent. Microscopically, the tumor consists of vascular elements in a connective tissue stroma, and is

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* Since this article was written Stout has reported a case of hemangio-endothelioma of the erector spinae muscles followed by evidences of lung metastases and symptoms of paraplegia four months after operation, and death after seven months. No autopsy findings were mentioned.

classified as cavernous, capillary, venous, or arterial.   Although pure types seldom exist, the cavernous variety is the most common.   Growth is by a multicentric proliferation of endothelial cells forming vascular channels with practically no tendency to anastomose with the normal vessels in the invaded tissue.   There are no proven cases of metastasis from a primary muscle hemangioma, although malignant degeneration has been reported as probable in a few instances.*

The diagnosis was correctly made in only 19 per cent of the cases, the difficulty being due mainly to the comparative rarity of the lesion and the depth of the tumor.   The history usually reveals a clinical onset early in life, often following trauma to the part, and pain of varying degree.   On physical examination, a mass, usually soft and often tender, sometimes changing in size and consistency with change of posture, is noted within the muscle.   The thigh is most commonly involved, especially the quadriceps femoris muscle.   Deformity and functional impairment are present in about one fourth of the cases.   The diagnosis may be confirmed by aspiration of blood from the tumor and by the presence of phleboliths on roentgenologic examination.   Angiography may also be employed as an adjunct in diagnosis or to evaluate the results of treatment.

In the differential diagnosis one must consider benign and malignant tumors, inflammatory lesions, and in some instances aneurysms.

The procedure of choice in treatment is early complete surgical excision well beyond the confines of the tumor, with good hemostasis, and with preservation or restoration of normal function of the part.   This was the treatment employed in 79 per cent of the cases, with improvement or cure in 90 per cent.   In cases in which malignant degeneration is suspected, postoperative deep roentgenotherapy is advocated.

There was no surgical mortality for the entire series.   Local recurrence or lack of improvement was reported in 6 per cent of the cases and postoperative deformity in 4 per cent.

Early diagnosis and wide surgical excision should aid in reducing postoperative recurrence, functional impairment, deformity, and the remote possibility of malignant degeneration.

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ACUTE RETROPERITONEAL ABSCESS AND PHLEGMON*

A STUDY OF SIXTY-FIVE CASES

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ACUTE RETROPERITONEAL INFECTIONS derived from a variety of sources have long been known to be grave lesions which at times present great difficulties both in diagnosis and in treatment. The earliest consideration of the subject was that of Abrille,[1] in 1854, who reported eight cases of suppuration in the retroperitoneal tissues. Since that early contribution, the literature is composed essentially of reports dealing with individual cases. Our purpose is to present a comprehensive consideration of infections of the retroperitoneal tissues with special reference to clinical classification, pathogenesis, clinical manifestations, diagnosis, and operative treatment. This paper is based on a study of 65 cases encountered on the Surgical Services of the Mount Sinai Hospital, New York, in the 18-year period from 1925 to 1942. We shall present 15 cases in summary† as the best means of illustrating the many problems involved.

CLASSIFICATION

An analysis of the 65 cases of acute retroperitoneal infections led to a simple classification on the basis of combined anatomic, pathologic, and clinical considerations. There was overlapping in some instances, but, in the main, the cases could be grouped. The classification is of clinical usefulness, and of special value in the decision as to the type of operative approach in the individual case. Infections limited to the extraperitoneal subphrenic space and to the extraperitoneal tissues of the pelvis are omitted from consideration; the former are more directly related to the problem of subphrenic abscess, and the latter are related to the rectum, bladder, prostate, and female pelvic organs. The classification of acute retroperitoneal infections is as follows:

A. Localized Form: Abscess
   1. Lumbar
   2. Iliac
   3. Subphrenic only (omitted from consideration)
   4. Pelvic only (omitted from consideration)
B. Diffuse Form: Phlegmon

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† The details of these cases will be published elsewhere at a later date.

LUMBAR RETROPERITONEAL ABSCESS

Anatomy.—The lumbar portion of the retroperitoneum (retroperitoneal space) extends from the twelfth dorsal vertebra and twelfth rib to the promontory of the sacrum and the iliac crest. The floor of the space is formed by the quadratus lumborum and psoas muscles.

The fascia covering the quadratus lumborum muscle is the anterior layer of the lumbodorsal fascia. This layer is not as strong as the middle and posterior layers. The fascia covering the psoas muscle has the following attachments: above, mesially, the body of the second lumbar vertebra; laterally, the first lumbar transverse process, thus forming a funnel-shaped opening communicating with the posterior mediastinum; mesial, the bodies of the lumbar vertebrae; lateral, the anterior layer of the lumbodorsal fascia; below, the iliac fascia. It is these fascial layers which tend to confine retroperitoneal abscesses to that space and thus render difficult their early recognition and surgical management.

The kidney lies on the fascia covering the quadratus lumborum and psoas muscles. The extraperitoneal areolar tissue is somewhat condensed to enclose the kidney, adrenal gland, and renal fat in a loose envelope called the renal fascia. At the outer border of the kidney the renal fascia divides into a prerenal and a retrorenal layer to envelop the kidney. The posterior layer, also called the fascia of Gerota, fuses with the fascia on the psoas and quadratus lumborum muscles. The anterior layer is much thinner and passing medially is lost in fat in front of the aorta. The two layers of the renal fascia fuse at the upper pole of each kidney, but separate again to enclose the corresponding adrenal gland. Above this they again unite and become continuous with the aponeurotic covering of the diaphragm. The layers fail to unite below and are lost in the fat near the iliac crest. The fat inside the renal fascia separates the renal fascia from the proper capsule of the kidney and is called the perinephric fat; the fat outside the retrorenal fascia is called the paranephric fat. Under exceptional circumstances suppuration derived from the kidney can extend into the retroperitoneal space instead of producing the customary perinephric abscess.

The fascial layers over the quadratus lumborum and psoas muscles are covered by areolar and fatty tissue which forms a bed for the kidney, ascending colon, and duodenum on the right, and the kidney and descending colon on the left. Numerous lymphatic vessels traverse the retroperitoneal areolar tissue with the well known grouping of lymph nodes about the great vessels.

Pathogenesis.—There were 25 cases of localized lumbar retroperitoneal infections. The sources of infection were as follows: Unknown (nine cases), distant focus (five cases), kidney (five cases), appendix (three cases), colon (two cases), and spine (one case). Although the source of infection was not determined in approximately one-third of the cases, the pathway of infection in such cases is probably *via* lymphatics in view of the rich lymphatic network traversing this region. On the other hand, it is not correct to describe

such cases as suppurative lymphadenitis unless suppurative lymph nodes are present. Thus, the lumbar retroperitoneal space was infected by direct extension from suppuration in an adjacent organ (kidney, appendix, colon, spine), by lymphatics, and by metastasis from distant foci of infection.

Trauma preceded the onset of symptoms in two cases of unknown etiology, and appeared to play a definite rôle in causation. The types of kidney lesions were multiple abscesses (two cases), calculous pyelonephritis (two cases), and carbuncle (one case). The primary suppurative foci in the metastatic cases were furuncles of the skin (two cases), acute pharyngitis (one case), chronic osteomyelitis of the femur (one case), and upper respiratory infection (one case).

Pathology.—In five of the cases of unknown etiology the abscesses lay under the lumbar aponeurosis of the transversalis muscle. The abscesses were immediately retroperitoneal, pushing the peritoneum forward, in three cases. In the remaining cases, the abscess was located within the psoas muscle.

In the cases of retroperitoneal suppuration derived from the kidney, the infection had spread beyond the confines of the perinephric fat and renal fascia into the retroperitoneal tissues. Infections within the renal fascia are perinephric and not retroperitoneal. From a consideration of the anatomy, it would seem that spread of infection beyond the renal fascia should occur most readily through the thinner prerenal layer, and inferiorly where the margins of the fascia do not unite. In our cases the spread of infection was anteriorly in two, inferiorly in one, posteriorly in one, and superiorly in one. In the latter case the upward spread continued above the diaphragm and involved the lung.

The metastatic abscesses varied in position: Three under the lumbar aponeurosis, one anterior to the kidney, and one in the psoas muscle. Two of the appendiceal abscesses presented under the lumbar aponeurosis, and the other pushed the peritoneum and ascending colon anteriorly; a retroperitoneal gangrenous appendix was found in the abscess in the latter case. In one of the cases of colonic origin the abscess was anterior to the kidney; a fishbone was found in the abscess. In the other case the abscess was secondary to a carcinoma of the colon and lay under the lumbar aponeurosis. The abscess derived from the spine was secondary to an osteomyelitis of the lumbar vertebrae and was similarly situated.

Bacteriology.—In the cases of unknown etiology the organisms cultured from the abscesses were *Staphylococcus aureus* in four, *Streptococcus hemolyticus* in one, *Staphylococcus albus* in one, and a mixture of *B. coli* and *Streptococcus viridans* in one. The organisms in the cases of renal origin were *Staphylococcus aureus* in two, *B. coli* in one, a mixture of *B. coli* and enterococcus in one, a combination of anaerobic staphylococcus and diphtheroids in one. The cultures of the metastatic abscesses secondary to furuncles of the skin and osteomyelitis of the femur were *Staphylococcus aureus*; in the cases secondary to acute pharyngitis and upper respiratory infection the organism was *Streptococcus hemolyticus*. *Bacillus coli* and a

mixture of *B. coli* and enterococcus were the organisms found in the appendiceal abscesses. The organism cultured from the abscesses of colonic origin was *B. coli*. In the case of spinal origin the organism was *Staphylococcus aureus*. Thus, the organisms varied with the source of infection, the *Staphylococcus aureus* and *B. coli* organisms predominating. It is perhaps significant that cultures from the abscesses of unknown origin grew chiefly staphylococci or streptococci, suggesting that they too may be metastatic.

Clinical Manifestations.—The ages of the patients ranged from ten months to 75 years; two cases occurred in children. The history of pain and fever was common to all patients. The pain was in the lumbar region in most cases, but in some instances it was elsewhere, such other locations being the hip, thigh, abdomen and chest. Other symptoms occasionally noted were chills, vomiting and loss of weight. Cough and foul sputum were noted in the patient with pulmonary suppuration. The duration of symptoms before admission to the hospital varied from four days to nine weeks, the average period being three to four weeks. In two cases there were preceding traumas; in one case immediately before the onset of symptoms, and in the other separated by a long free interval.

On examination, there was tenderness in and spasm of the lumbar muscles on the affected side in 23 cases. This was associated with a tender mass in 16 cases, palpable in the lumbar region in nine patients and in the abdomen in seven cases. In two patients there were tender abdominal masses not associated with lumbar tenderness. There was marked abdominal distention in two cases of renal origin. The abdominal masses were usually large and located in the hypochondrium. Psoas (hip) spasm was noted in five patients.

Fever was a constant finding during the period of observation, usually between 102° and 103° F., and associated with an increase in pulse rate. A constant laboratory finding was leukocytosis, averaging 21,600 white blood cells. There was usually an associated polymorphonucleosis, averaging 80 per cent. One or more negative blood cultures were reported during the period of observation in ten patients in whom they were taken. In one case, in which the infection was secondary to multiple abscesses of the kidney, the blood culture was positive for *Staphylococcus aureus*.

Diagnosis.—Although the combination of lumbar pain, tenderness in and spasm of the lumbar muscles, a mass (lumbar or abdominal), fever, and leukocytosis is diagnostic of lumbar retroperitoneal abscess, all these criteria may not be present in the earlier phases. The absence of a mass may lead to protracted observation, and we stress the value of an examination under anesthesia in cases in which muscle spasticity exists and apparently interferes with the palpation of a mass.

The nature of the lesion was often not suspected on admission to the hospital. This is borne out by the fact that the periods of preoperative observation varied from one day to one month, the average period being ten days. Occasionally a suppurative lesion was not considered, the diagnosis of neo-

plasm of the kidney being made in one patient, and intra-abdominal malignancy in another. The presence of a large mass in the hypochondrium was misleading in both cases.

In the cases of renal origin cystoscopic and pyelographic findings were negative when the source of infection was a cortical abscess or carbuncle. Occasionally, as in two of our cases, roentgenograms of the spine may show a scoliosis of the lumbar spine with convexity away from the diseased side and an obscured psoas margin, a finding noted by Beer[2] in the roentgenologic examination of perinephric abscess. A common error is to suspect a perinephric abscess when the abscess has no such relationship to the kidney.

Treatment and Results.—Operation was performed in all cases; in 21 cases the abscesses were drained through lumbar incisions, and in four cases through the transperitoneal route. Extraperitoneal drainage is, of course, advised, and in the cases in which the peritoneal cavity was traversed the diagnosis of a retroperitoneal abscess had not been made before operation. One of the two deaths in this group was due to peritonitis following transperitoneal drainage. It is for this reason that emphasis should be placed upon a final examination under anesthesia just before operation for an abscess or an inflammatory mass whose relationship to the retroperitoneal space is doubtful. If the peritoneal cavity is traversed accidentally, it would be advisable to close the peritoneum and then proceed with lumbar drainage. However, with a careful operative technic and the addition of sulfonamides, peritonitis may be avoided. In doubtful cases the lumbar incision is preferable and can be used with advantage for drainage of intraperitoneal abscesses in contiguity with the posterior parietal peritoneum.

The operative incision to be employed for a lumbar retroperitoneal abscess is one which can be termed the anterior half, or more, of the customary incision for exposure of the kidney. Special care should be taken to avoid injury to the twelfth thoracic nerve. The situation of the incision must be placed in relationship to the mass. No difficulty in entering the abscess is encountered where the abscess lies just under the lumbar aponeurosis, but where the abscess is situated more mesially in proximity to the posterior peritoneum the incision must be deepened to the peritoneum. The latter, under clear visualization, is stripped away and retracted toward the midline as the exposure is deepened in order to approach the mass.

Adequate drainage, particularly in multilocular abscesses, is necessary. By this we mean unroofing the abscess, evacuating its contents, inserting retractors, and fully visualizing all its recesses. This is followed by drainage by gauze placed as a packing, or packings, to the limits of the infection. The type of operation which terminates with the introduction of a drainage tube as soon as pus is encountered is apt to be followed by untoward complications and sequelae. Tube drainage should be reserved for those exceptional instances in which adequate unroofing of the abscess would damage important structures. In this group drainage of the abscesses resulted in fairly prompt subsidence of the clinical manifestations. On

an average, the patients were discharged from the hospital one month after operation.

Five patients were readmitted to the hospital for the treatment of conditions related to the retroperitoneal abscesses. Further operative procedures were appendicectomy (two cases), nephrectomy (one case), and repair of incisional hernia (one case). In one patient there was recurrence of abdominal pain and fever and persistence of the mass; further operation was not necessary.

In this group of 25 cases there were two deaths, a mortality of 8 per cent. One death occurred in a ten-month-old child with a small abscess between the kidney and the descending colon. Death was attributable to peritonitis secondary to transperitoneal drainage. The second fatality was in a 50-year-old woman with a large retroperitoneal abscess secondary to abscesses of the kidney; the patient died 36 hours after operation.

Twelve patients were followed for more than one year after operation, and were well.

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COMMENTS ON FIVE ILLUSTRATIVE CASES
REPRESENTATIVE OF GROUP A-1*

GROUP A-1—LUMBAR RETROPERITONEAL ABSCESS

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Case 1.—*Trauma. Slow evolution of lumbar abscess. Drainage. Recovery.*

COMMENT: The slow evolution of a lumbar retroperitoneal abscess over a period of six weeks following a fall on the hip is noteworthy. The patient was in the hospital under observation for 18 days before operation.

Case 2.—*Furunculosis. Psoas abscess. Drainage. Recovery.*

COMMENT: The clinical manifestations were those of a perinephric abscess following furunculosis, but at operation there was no evidence of infection in or around the kidney. The abscess lay within the substance of the psoas muscle.

Case 3.—*Carbuncle of kidney. Retroperitoneal abscess. Drainage. Recovery.*

COMMENT: The signs of peritoneal irritation were related to the close approximation of the abscess to the peritoneum. A review was made of 100 cases of perinephric abscess, and this was the only one in which the abscess was between the kidney and the posterior peritoneum.

Case 4.—*Retroperitoneal appendiceal abscess. Transperitoneal drainage. Recovery.*

COMMENT: Operation was transperitoneal in this case because the diagnosis was appendiceal abscess. Although a large, foul, retroperitoneal abscess was drained through this approach, there was no infection of the peritoneum after operation. Drainage of a retroperitoneal abscess through the peritoneum is not advised (death in another case was due to peritonitis after such an

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* The details of these cases will be published elsewhere at a later date.

approach), but with a careful operative technic and the addition of sulfonamides infection of the peritoneum is not anticipated.

Case 5.—*Foreign body (fishbone) abscess. Preoperative Diagnosis: Neoplasm of kidney.*

COMMENT: The preoperative diagnosis was neoplasm of the kidney, the onset of fever and tenderness being associated with supposed necrosis of the tumor. The colon was not visualized at operation but the fishbone probably migrated through a small perforation in the bowel.

ILIAC RETROPERITONEAL ABSCESS

The first description of iliac retroperitoneal abscess was that of Pegram[12] in 1903, who reported operations in two children for acute iliac adenitis. Since that contribution, 145 cases of iliac abscess have been reported in the literature (Largos García,[7] Hyman,[4] Frank,[3] Irwin,[5] McCorkle and Stevenson,[8] and Ladd and Gross[6]). These reports (with the exception of the case of McCorkle and Stevenson which was an appendiceal abscess) were of cases of acute iliac adenitis. As will be brought out later, our criteria for classification of cases in this group are more strict and are confined to cases in which infections draining into such lymph nodes were demonstrable and acutely inflamed lymph nodes were present. In many reports the diagnosis is assumed and is not proved by operative findings, whereas in our cases abscesses were drained. Not all cases of acute iliac lymphadenitis go on to suppuration and abscess formation, and abscesses alone are considered by us in this classification.

A review of the literature reveals that the majority of cases of acute iliac lymphadenitis occurs in childhood. There has been a variable percentage of recoveries without operation. In the group of Ladd and Gross there were 35 cases in childhood, 17 of which subsided under conservative therapy. The average operative mortality of all cases in the literature was 5 per cent.

Anatomy.—In the iliac fossa the psoas and iliacus muscles are separated from the retroperitoneal tissues by the thick iliac fascia. Laterally, this fascia is fixed to the iliac crest; mesially, it is attached to the brim of the true pelvis at the ileopectineal line. The iliac and transversalis fasciae become continuous with each other at the part of the inguinal ligament which is lateral to the external iliac vessels, and are firmly attached to the ligament. In the region of the external iliac vessels they pass downwards beneath the inguinal ligament, the transversalis fascia in front of, and the iliac fascia behind, the vessels. Thus, the pathway of infection from the iliac fossa to the upper thigh becomes evident. In the thigh the fasciae form a sheath for the femoral artery and vein.

In the retroperitoneal tissues of the iliac fossa are the ureter, the spermatic or ovarian vessels, and the genitofemoral nerve. The external iliac artery is separated from the psoas muscle behind and laterally by the iliac fascia. The external iliac lymph nodes form three chains around the external iliac vessels. The external iliac nodes receive lymphatics from the inguinal nodes,

the glans penis, the umbilicus, the lower part of the abdominal wall, the vagina, the uterine cervix, the prostate, the bladder, the membranous portion of the urethra, and the internal iliac nodes. The genitofemoral nerve passes obliquely through the psoas muscle and descends on the surface of the muscle.

Pathogenesis.—There were 23 cases of localized iliac retroperitoneal infections. The sources of infection were as follows: Unknown (eight cases), acute iliac lymphadenitis (five cases), appendix (three cases), metastatic (two cases), sigmoid colon (two cases), uterus (two cases), and ureter (one case). The cases of acute iliac lymphadenitis were those in which infections draining into such lymph nodes were present and acutely inflamed lymph nodes were demonstrable. Considering the extensive lymphatic drainage into the external iliac lymph nodes, the likelihood of a small primary focus of infection being overlooked, and the difficulty of identifying lymph nodes in an abscess because of necrosis, it would probably be correct to include some of the cases of unknown etiology in the group of iliac adenitis. Thus, the iliac retroperitoneal space was infected by direct extension from suppuration in an adjacent organ (appendix, sigmoid colon, uterus, ureter), by lymphatics, and by metastasis from distant foci of infection.

Trauma preceded the onset of symptoms and appeared to play a definite rôle in causation in four cases of unknown etiology, and in one case of acute iliac lymphadenitis. In two of these cases infected hematomas were present. Infections of the foot and thigh were the primary sources of infection in four cases. The metastatic infections originated in mastoid suppuration. The sigmoid lesions were in one case diverticulitis, and in the other a perforation of unknown etiology. The appendiceal lesions were retroperitoneal appendiceal abscesses. The cases of uterine origin occurred postpartum, and after vaginal operation for uterine prolapse. Multiple operations for ureteral calculi, years before, preceded the infection of ureteral origin.

Pathology.—In the cases of unknown etiology the abscesses were well localized; five were located within, or in close contact with, the psoas muscle. In the four cases of acute iliac lymphadenitis secondary to infections of the lower extremity, the lower limit of infection was at the inguinal ligament; acutely inflamed lymph nodes were found within, or in close proximity to, the abscesses.

The appendiceal abscesses were well localized in the retroperitoneal iliac region but in no case was the appendix visualized at operation. The abscess secondary to perforation of the sigmoid was of unusual interest because of the extraordinary extent of the infection: downward, behind the femoral vessels into the thigh; backward, into the pelvis; outward, through the sacrosciatic foramen into the gluteal region. The infection following operation for prolapse of the uterus was unusual in that it was bilateral, involving the iliac retroperitoneal spaces on both sides.

Bacteriology.—In the cases of unknown etiology the organisms cultured

from the abscesses were *Streptococcus hemolyticus* in five, *Staphylococcus aureus* in two, and *Streptococcus viridans* in one. The organisms in the cases of acute iliac lymphadenitis were *Streptococcus hemolyticus* in three, and *Staphylococcus aureus* in two. The cultures of the metastatic abscesses were *Streptococcus hemolyticus* in one, and pneumococcus (Type-19) in one, *Bacillus coli* was the organism in the cases of appendiceal abscess and diverticulitis of the sigmoid. The culture of the perforation of the sigmoid was a mixture of *B. coli,* enterococcus, and *Streptococcus viridans.* Enterococcus was the organism found in the abscess following operation for uterine prolapse. A mixture of enterococcus and *B. coli* was the culture of the abscess of ureteral origin. Thus, as in the lumbar retroperitoneal abscesses, the organisms varied with the source of infection, the *Streptococcus hemolyticus* and *B. coli* organisms predominating.

Clinical Manifestations.—The ages of the patients ranged from seven months to 62 years. Two groups occurred only in children—the cases of unknown etiology, and the metastatic abscesses. Four of the five cases of acute iliac lymphadenitis were in children. Thus, the iliac type of retroperitoneal suppuration is common in childhood.

All patients complained of pain, located in the abdomen (13 cases), and in the lower extremity (ten cases). Abdominal pain was noted either in the lower abdomen (iliac region), or in the inguinal region. The pain in the lower extremity was referred to the hip, thigh, or knee. This was particularly true of abscesses involving the psoas muscle, the referred pain being due to direct irritation of branches of the lumbar plexus.

Fever was noted in the histories of 15 cases, and chills in three cases. The duration of symptoms before admission to the hospital varied from two days to five months, the average period being three to four weeks. In five cases there were preceding traumas, within 48 hours of the onset of symptoms in three cases.

The most common feature of physical examination was tenderness either in the iliac or inguinal regions. A mass was found in these regions in 15 cases and in three other cases an indefinite mass was noted. In seven instances there were positive findings on rectal examination, either a tender fullness or a mass. In one case the only lead was a tender mass felt on rectal examination. The finding of psoas (hip) spasm was an important sign and was present in 11 cases. It should be noted that the signs referred to above were found at some time in the period of observation, but were not always present on admission to the hospital.

Fever was a constant finding during the period of observation, usually between 102° and 103° F., with an associated increase in pulse rate. Leukocytosis and polymorphonucleosis were noted in 18 of the 19 cases in which blood counts were recorded, averaging 19,000 and 82 per cent, respectively. One or more negative blood cultures were reported during the period of observation in five cases in which they were taken. In one of the metastatic

abscesses secondary to mastoid suppuration the blood culture was positive for *Streptococcus hemolyticus*.

Diagnosis.—In view of the frequency of iliac retroperitoneal abscesses and diseases of the hip joint (acute infectious arthritis and tuberculosis) in childhood, the differentiation between these unrelated lesions becomes at times a problem only insofar as pain in the lower extremity and hip spasm are common to both. As far as the latter is concerned, motion of the hip in iliac abscess is limited to extension, whereas in disease of the hip joint the hip is partially restricted in all directions.

A suppurative lesion was usually suspected because of fever and local tenderness, but the slow evolution of a mass often delayed diagnosis. Operation was sometimes withheld until a mass became evident. As a result the preoperative period of observation ranged from one day to one month. Some of the lesions were found to be in an advanced state of suppuration at the time they came to operation. Therefore, as has been suggested for lumbar retroperitoneal abscess in cases in which a mass cannot be felt, examination under anesthesia may reveal a mass which could not be felt through the spastic lower abdominal wall. Three of the cases of unknown etiology were erroneously diagnosed as acute appendicitis. In two cases, in which the abscesses were in close proximity to the psoas muscle, roentgenograms of the spine revealed a scoliosis in the lumbar region with convexity away from the diseased side.

Treatment and Results.—Operation was performed in all cases; in 19 cases the approach was extraperitoneal, and in four cases transperitoneal. The infections, usually appendiceal abscesses, were considered to be intraperitoneal before operation in the cases in which the peritoneum was traversed. This not only reveals the margin of error in diagnosis, but also serves to emphasize the necessity for being prepared for the surprise of encountering an extraperitoneal abscess when an intraperitoneal one is anticipated. Death from peritonitis will be avoided by a careful operative technic to avoid peritoneal contamination should the abscess be encountered inadvertently, or, when the lesion is found to be extraperitoneal before pus is encountered, by a new incision for its extraperitoneal approach. This statement is supported by the fact that there was neither peritoneal infection nor death in the cases in which the peritoneum was traversed.

An inguinal incision was employed in most of the cases of iliac retroperitoneal abscess. This has the advantage of liberal extension laterally and upwards in order to expose more completely a deeply placed abscess or to explore for a suspected one. The incision is placed directly above and parallel to the inguinal (Poupart's) ligament, and traverses the external oblique aponeurosis, the internal oblique muscle, and the transversalis fascia. Thereby, the lateral portion of the inguinal canal is laid open. The peritoneum is stripped, as in the approach to the pelvic ureter, upward and medially away from the iliac fascia.

The need of full operative visualization and adequate drainage, discussed in the management of lumbar retroperitoneal abscess, must be emphasized. Inadequate drainage is prone to be followed by complications and sequelae, as illustrated in Case 6 (to follow). The abscesses lying within, or in close contact with, the psoas muscle, because of their depth and proximity to the external iliac artery, may present difficulties in exposure. Drainage of such an abscess necessitated in one case (Case 6) severance of the psoas muscle. One of the two deaths in this group was attributed to inadequate drainage, as evidenced by continued fever, hip spasm, unhealthy appearance of the wounds, and leukocytosis.

The average period of postoperative hospitalization was four weeks. Although the period of preoperative observation was long in the cases of iliac lymphadenitis, healing after operation was most rapid in these cases.

In this group of 23 cases there were two deaths, a mortality of 8.7 per cent. One death, in a child, has been referred to. The second fatality was in a 57-year-old man with an iliac abscess secondary to perforation of an inflamed diverticulum of the sigmoid. Although the abscess cavity was clean, at postmortem examination there were a number of small abscesses in an inflammatory mass involving the sigmoid, omentum, and a loop of ileum.

Ten patients were followed for more than one year after operation, and were well.

COMMENTS ON FIVE ILLUSTRATIVE CASES
REPRESENTATIVE OF GROUP A-2*

GROUP A-2—ILIAC RETROPERITONEAL ABSCESS

Case 6.—*Trauma. Recurrent acute and chronic iliac retroperitoneal abscesses requiring multiple drainage. Recovery.*

COMMENT: An iliac retroperitoneal abscess, preceded by a fall on the back, was drained and healed three months after operation. The abscess recurred following repeated trauma one year and eight months later. Inadequate drainage necessitated a fourth operation in which infection was found anterior, posterior, and mesial to the psoas muscle. For adequate drainage severance of the psoas muscle was required.

Case 7.—*Foot infection. Suppurative lymphadenitis. Slow evolution of iliac abscess. Drainage. Recovery.*

COMMENT: The sequence of events were infection of the foot, lymphangitis and lymphadenitis of femoral, inguinal and iliac nodes, and iliac retroperitoneal abscess. The slow evolution of the abscess, over a period of three weeks, is worthy of note. The retroperitoneal mass was never well defined.

Case 8.—*Iliac appendiceal abscess. Transperitoneal drainage. Recovery.*

COMMENT: This case is classified as an iliac appendiceal abscess because of the clinical manifestations and operative findings, although the appendix

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* The details of these cases will be published elsewhere at a later date.

was not seen at operation. Although there was no fecal discharge from the wound, a transient fistula into the cecum was demonstrated by injection of lipiodol.

Case 9.—*Perforation of sigmoid. Extensive retroperitoneal infection involving iliac retroperitoneal space, pelvis, thigh and gluteal regions, requiring multiple drainage and closure of sigmoidal perforation. Recovery.*

COMMENT: This case is of interest because of the extraordinary extent of the infection secondary to perforation of the sigmoid, not only involving the iliac retroperitoneal space, but the pelvis, thigh and gluteal regions. Multiple operations, over a period of two and one-half years, were necessary before cure was effected. The etiology of the perforation was not determined.

Case 10.—*Vaginal operation for prolapse of the uterus and cystorectocele. Bilateral ilias retroperitoneal abscesses. Bilateral drainage. Removal of pyosalpinx. Recovery.*

COMMENT: This case is unique, in that the iliac retroperitoneal suppuration was bilateral. The clinical picture at the time of drainage was that of advanced peritonitis. Later observation revealed that tubal suppuration also followed the original pelvic operation.

DIFFUSE RETROPERITONEAL INFECTIONS (PHLEGMON)

The diffuse, phlegmonous, retroperitoneal infections stand out in striking contrast to the previously described localized abscesses. This difference is noted not only in the pathologic and clinical features, but in the operative results.

The reaction of the retroperitoneal tissues to infection was studied experimentally by Meyer,[9] and the results of these experiments tend to prove that the retroperitoneal tissues are less resistant to the invasion of organisms than the peritoneum. In ten dogs, no deaths occurred from intraperitoneal injections of cultures of *Staphylococcus aureus* and *B. pyocyaneus*, except immediate deaths from toxemia, and in these, three of five had sterile peritoneal cavities; no abscesses developed; and there were no signs of peritonitis. In 15 dogs receiving retroperitoneal injections of the same organisms, one-third of the animals in which staphylococcus was used developed abscesses, and three-fourths of those in which pyocyaneus was used developed abscesses, all of whom died.

Pathogenesis.—There were 17 cases of diffuse retroperitoneal infection. The sources of infection were as follows: Appendix (six cases), kidney (two cases), ileum (two cases), colon (one case), pancreas (one case), uterus (one case), esophagus (one case), spine (one case) ischiorectal infection (one case), and unknown (one case). In contrast to retroperitoneal abscesses, in which the etiology was unknown in one-third of the cases, the source of infection could almost always be stated.

The type of lesion in the six cases of appendiceal origin was perforated gangrenous appendicitis in five cases, and phlegmonous appendicitis in one case.

In four cases the appendix was described as retrocecal, and in two cases retrocecal and retroperitoneal.

Abscesses of the kidney were the lesions of renal origin. The remaining pathologic conditions were as follows: Advanced regional ileitis, with perforation; carcinoma of the descending colon, with perforation; acute necrotizing pancreatitis; postabortive endometritis and parametritis; traumatic perforation of the distal end of the esophagus; osteomyelitis of the lumbar vertebrae; and infected wound of the ischiorectal region.

Pathology.—The essential pathologic picture of diffuse retroperitoneal infections is a phlegmonous or necrotizing inflammation, without walling-off, of the retroperitoneal tissues. This is represented by fibrinopurulent or necrotic exudate and small collections of pus. The most striking features of these diffuse infections are the extent of spread and the ill-defined limits.

In all instances the lumbar retroperitoneal tissues were involved. The infection reached the diaphragm in 11 patients, forming subdiaphragmatic abscesses in three cases. In three patients the spread of infection continued above the diaphragm. This upward spread involved the posterior mediastinum (three cases), the pleura (one bilateral) (two cases), and the pericardium (one case).

The infection involved the iliac retroperitoneal tissues in 11 instances. In three patients the infection continued downwards, involving the thigh in two cases, and the inguinal, scrotal and ischiorectal regions in the remaining case. The pelvic retroperitoneal tissues were involved in four cases.

Bacteriology.—*Bacillus coli* was the predominating organism. In seven cases it was found alone; in combination with staphylococcus in one, enterococcus in one, enterococcus and *Cl. welchii* in one, enterococcus and *B. proteus* in one, and *B. pyocyaneus* and *nonhemolytic Streptococcus* in one. A combination of enterococcus and Friedländer bacillus was found in one case. *Streptococcus hemolyticus* was the organism in one case.

Clinical Manifestations.—The ages of the patients varied from 20 to 62 years, and the infection is thus a lesion of adult life. The symptoms at the onset were those of the underlying disease. In the cases of appendiceal origin, the unusual features were right upper quadrant abdominal pain and chills in two cases. Lumbar pain, chills, and fever were the symptoms in the cases of renal origin. In the cases in which there was extension of infection to the thigh and scrotum, there was pain in these regions.

The outstanding symptoms in the patients with regional ileitis were abdominal pain and fever in one, and pain in the hip radiating down the thigh in the other. The symptoms in the other cases were as follows: Carcinoma of the colon: Lumbar pain and fever. Pancreatitis: Generalized abdominal pain and vomiting. Parametritis: Pain in the back, chills, and fever. Perforation of the esophagus: Epigastric pain, chilliness, fever, dyspnea, and cough. Osteomyelitis of the lumbar vertebrae: Lumbar pain and fever. Ischiorectal infection: Lower abdominal pain, fever, chills, and vomiting. Unknown etiology:

Abdominal pain and distention, fever, and chills. Thus, in only one-fourth of the cases did the symptoms suggest a retroperitoneal infection.

The duration of symptoms varied from one day to ten weeks. The period was less than one week in five cases of appendicitis and in the cases of carcinoma of the colon, pancreatitis, perforation of the esophagus, and ischiorectal infection. The duration of symptoms was longest in the cases of ileitis, in those of renal origin, and in the osteomyelitis of the lumbar vertebrae.

The findings on physical examination were usually those of the underlying disease. Occasionally, signs were present which suggested retroperitoneal infection. Thus, in the cases of appendicitis, lumbar tenderness was noted in three patients, and a tender lumbar mass in one patient; tender lumbar masses in the cases of renal origin and carcinoma of the colon; lumbar tenderness in the case of parametritis. Often, however, signs of retroperitoneal infection were absent. In the cases in which there was extension of infection to the thigh, scrotum, and ischiorectal region, there were signs of suppuration in these areas. Abdominal distention was a frequent finding. Psoas (hip) spasm was noted in four patients; in the cases of ileitis, in one case of renal origin, and in the instance of osteomyelitis of the lumbar vertebrae.

Fever was a constant finding during the period of observation, usually above 102° F., with an associated increase in pulse rate. Leukocytosis and polymorphonucleosis were present in 12 of the 14 cases in which blood counts were recorded, averaging 16,000 and 83 per cent, respectively. One or more negative blood cultures were reported during the period of observation in eight cases in which they were taken. The blood cultures were positive in two cases—*B. coli* in one case of renal origin and *Streptococcus hemolyticus* in the case of ischiorectal infection.

Diagnosis.—There were two general features which could be regarded as suggestive of a diffuse retroperitoneal infection: First, the patients were ill out of proportion to the manifestations ordinarily referable to the causative infective focus; and second, pronounced abdominal distention was common. The diagnosis of a retroperitoneal infection was not made in 11 cases. In the six cases in which the diagnosis was made the extent of infection was not realized. Thus, in the cases of appendiceal origin, the diagnoses were acute appendicitis in three, appendiceal abscess in one, acute cholecystitis in one, and perinephric abscess in one. Retroperitoneal infection was not considered in the cases of pancreatitis, parametritis, ischiorectal infection, in one case of ileitis and in the case of unknown etiology. In addition to the cases of renal origin the diagnosis of retroperitoneal infection was made in the cases of perforation of the esophagus, carcinoma of the colon, osteomyelitis of the lumbar vertebrae, and in one case of ileitis. The periods of preoperative observation were short: Under 24 hours in five; 24 to 48 hours in five; two days in one; eight days in one; 12 days in one; and 16 days in one.

Treatment and Results.—Operation was performed in 14 cases. The operative approach was usually for the underlying disease: transperitoneal, in five cases of appendiceal origin, in one case of ileitis, and in the cases of pancreatitis, perforation of the esophagus, and in the case of unknown etiology; extraperitoneal, in the cases of renal origin, in one case of ileitis, in the carcinoma of the colon, and in the osteomyelitis of the lumbar vertebrae. In the cases in which there was spread of infection to the thigh, scrotum, and ischiorectal region, additional incisions were made in those regions.

In this group of 17 cases there were 17 deaths, a mortality of 100 per cent. The duration of life after operation was as follows: Under 24 hours in three; 24 to 48 hours in four; four days in one; five days in one; six days in one; two weeks in one; four weeks in one; and seven weeks in two. The period of hospitalization in the three fatal unoperated cases was 30 hours in one patient; and four days in each of two patients.

The primary cause of mortality was the extent of infection which precluded adequate drainage, such as spread of infection to the posterior mediastinum, pericardium, root of the mesentery of the small intestine, and bilateral infections. In cases in which such spread did not take place, the infections often extended from the diaphragm downward through the lumbar and iliac retroperitoneal tissues. Infections of appendiceal origin should offer a better prospect for recovery. The diagnosis is usually made early and the infection can usually be adequately drained, although this was not true of the cases in this series, the extent of infection found at postmortem examination being greater than that which existed at the time of operation. In two cases peritonitis and abdominal wall infection, which did not exist at the time of operation, contributed to the fatal issue. The type of drainage is very important, namely, drainage by gauze placed as a packing to the limits of the infection. The experience with sulfonamide drugs was limited to three cases in this group, but their administration did not influence the course of the disease.

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COMMENTS ON FIVE ILLUSTRATIVE CASES
REPRESENTATIVE OF GROUP B[*]

GROUP B—DIFFUSE RETROPERITONEAL INFECTIONS (PHLEGMON)

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Case 11.—*Retroperitoneal appendiceal abscess. Drainage. Retroperitoneal phlegmon. Death.*

COMMENT: The patient presented a retroperitoneal appendiceal abscess at operation. The institution of adequate drainage (see Case 4) might have resulted in recovery. The extent of infection found at postmortem examination was greater than at operation.

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[*] The details of these cases will be published elsewhere at a later date.

Case 12.—*Abscesses of kidney, with retroperitoneal phlegmon. Drainage. Death.*

COMMENT: This case illustrates the rapid spread of a phlegmonous retroperitoneal infection to the scrotum, perineum and ischiorectal region.

Case 13.—*Regional ileitis, with retroperitoneal abscesses and phlegmon. Multiple drainage. Death.*

COMMENT: The earliest manifestation of advanced regional ileitis (except for occasional diarrhea) was a retroperitoneal abscess secondary to perforation of the ileum. The abscess was one of several, and there was a phlegmonous inflammation in both retroperitoneal spaces which extended downward into the pelvis on both sides, passing through the greater sciatic notches into the gluteal regions and thighs.

Case 14.—*Carcinoma of colon, with retroperitoneal abscess and phlegmon. Drainage. Death.*

COMMENT: The patient had a carcinoma of the descending colon, with perforation, resulting in a retroperitoneal abscess and phlegmon. The retroperitoneal infection was bilateral.

Case 15.—*Endometritis and parametritis, with retroperitoneal phlegmon. No operation. Death.*

COMMENT: This is a case of phlegmonous retroperitoneal infection derived from a suppurative endometritis and parametritis, with rapid evolution of the infection and death.

SUMMARY AND CONCLUSIONS

A study of acute retroperitoneal infections has been based on an analysis of 65 cases. These infections have been classified as abscesses occurring in the lumbar or iliac regions and phlegmonous inflammations diffusely spread in the retroperitoneal tissues. There were 25 lumbar abscesses, 23 iliac abscesses, and 17 diffuse infections.

Acute retroperitoneal infections are always secondary. The infection is derived by direct extension from suppuration in an adjoining organ, by lymphatics, and by metastasis from distant foci of infection. The etiology was not determined in one-third of the abscesses, whereas the source of diffuse infections could almost always be stated. Trauma appeared to play a definite rôle in causation in 15 per cent of the abscesses. The most common source of diffuse infections was acute appendicitis (35 per cent).

There is a marked contrast between the pathologic features of abscess and phlegmon of the retroperitoneal tissues. The former is well-localized, and the latter is represented by fibrinopurulent or necrotic exudate and small collections of pus, with a tendency to spread beyond the confines of the retroperitoneum.

The bacteriology varied with the source of infection, the *Staphylococcus aureus, Streptococcus hemolyticus,* and *B. coli* predominating in the abscesses, and the *B. coli* alone or in combination, in the diffuse infections.

Iliac abscesses occur more frequently in childhood—61 per cent of the cases in this study.

A history of pain and fever was common to all patients with retroperitoneal abscesses. Pain in the lower extremity was noted in about one-half of the cases of iliac abscess, particularly abscess involving the psoas muscle. The symptoms in the diffuse infections were masked by those of the underlying disease, and in only one-fourth of the cases did symptoms suggest a retroperitoneal infection. Tenderness in, and spasm of, musculature in the region of abscesses was a common feature, associated with a mass in 65 per cent of the cases. Abdominal examination revealed a mass in one-half of the cases of lumbar abscess. Psoas (hip) spasm was noted in one-half of the cases of iliac abscess.

A suppurative lesion was usually suspected, but the slow evolution of a mass often delayed the diagnosis of retroperitoneal abscess. Operation was sometimes withheld until a mass became evident; some of these lesions were found to be in an advanced state of suppuration at operation. Examination under anesthesia is suggested in cases in which muscle spasticity exists and interferes with the palpation of a mass. There were two general features suggestive of diffuse retroperitoneal infections, toxicity and abdominal distention. The diagnosis of retroperitoneal infection was not made in 65 per cent of the cases of diffuse infection, and in the cases in which the diagnosis was made the extent of infection usually was not realized.

The operative approach was extraperitoneal in 83 per cent of the abscesses, and in the cases in which the peritoneal cavity was traversed the diagnosis of a retroperitoneal abscess had not been made before operation. A careful operative technic will avoid peritoneal contamination should the abscess be encountered inadvertently, or, when the lesion is found to be extraperitoneal before pus is encountered, by a new incision for its extraperitoneal approach. The need of full operative visualization and adequate drainage is emphasized and the details of operative technic are discussed.

There was a wide difference in the operative mortality of abscesses and diffuse infections—8 per cent in abscess and 100 per cent in diffuse infection. The primary cause of death in diffuse infections was the extent of infection which precluded adequate drainage.

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ANNULAR PANCREAS PRODUCING DUODENAL OBSTRUCTION*

REPORT OF A SUCCESSFULLY TREATED CASE

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THERE has recently come under our care a newly born infant with evidence of duodenal obstruction, which was proved to be due to an annular pancreas. Operation on the third day of life has brought about complete relief of the baby's symptoms. Both the rarity of this congenital abnormality and its successful correction by surgical means have prompted us to make the following presentation:

Case Report.—S. M., a three-day-old female infant, was referred to the Children's Hospital by Dr. Dorothea Moore on September 16, 1942, because of persistent vomiting of two days' duration. During the mother's pregnancy there had been a moderate hydramnios. The infant was delivered at full term after a short, uncomplicated labor. The birth weight was 5 lbs. 12 oz.

Four hours after birth the baby passed a normal-appearing meconium stool. Shortly after this she vomited. During the remainder of the first 24-hour period there was vomiting on four occasions. At no time was the vomitus bile-stained. On the second day the baby was put to the breast, and suckled well, but there was projectile vomiting of curdled milk after each nursing. Again, there was no bile staining. Two meconium stools were passed. On the third day of life, the course was essentially the same, and was characterized by repeated vomiting and by the passage of only a small amount of meconium by rectum.

Physical examination on entry showed a small but normally developed infant, as far as external appearances were concerned. Temperature 100.4° F. Pulse 140. Respirations 30. There was slight dehydration. The upper abdomen, while not greatly distended, was distinctly more prominent and tympanitic than the lower abdomen, which was flat and soft. Large peristaltic waves, apparently gastric in origin, could be seen running across the epigastrium from left to right. No abnormal masses could be palpated. On auscultation, no abnormal peristalsis could be detected.

Roentgenologic examination of the abdomen, with the child in the recumbent position, showed some dilatation of the stomach, and a bubble of gas in the right upper quadrant of the abdomen which was assumed to be air in a dilated first portion of the duodenum (Fig. 1). No gas could be found in any other part of the abdomen. These findings were interpreted as representing a complete obstruction of the duodenum. A barium meal was not given. It was felt that the diagnosis of duodenal obstruction was sufficiently established to warrant surgical exploration without further investigation.

Operation was undertaken after infiltrating the anterior abdominal wall with 0.5 per cent procaine hydrochloride. During the procedure the child was allowed to suck on a nipple containing sugar water and brandy. A long, right rectus incision was made, retracting the muscle belly laterally. Upon opening the peritoneum, about one ounce

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of straw-colored fluid escaped. The first part of the duodenum was strikingly dilated to four or five times its normal size. This enlargement extended downward to the second part of the duodenum, which was markedly constricted by a ring of pancreatic tissue which completely surrounded the duodenum and which was continuous with the head of the pancreas (Fig. 2). Below this site the small intestine was quite collapsed and was no more than 5–6 Mm. in diameter. Since a few bubbles of gas could be felt
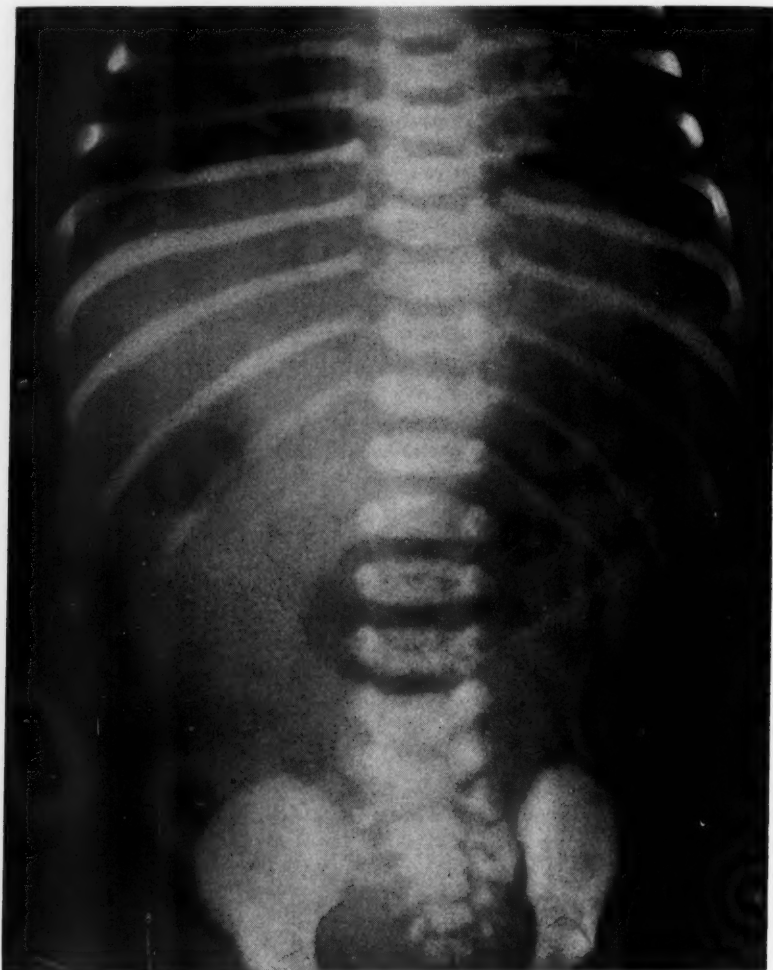

FIG. 1.—Roentgenogram of three-day-old baby with duodenal obstruction from annular pancreas. Note gas in the stomach and in the dilated first portion of the duodenum. No gas seen in remainder of abdomen.

in this tiny intestine, it was thought that the duodenal obstruction was not a complete one. However, the lumen at its constricted area was certainly no more than a millimeter or two in diameter. The gallbladder, hepatic duct, and upper portion of the common duct were normal in appearance and were not distended. It was, therefore, felt that the lower end of the common duct was not obstructed, even though this structure could not be fully traced behind the duodenum and its relationship to the ring of pancreatic tissue could not be determined. There was an incomplete rotation of the colon; the cecum and appendix lay in the midepigastrium, while the exposed duodenum ran directly

down the right paravertebral gutter to join the jejunum. This state of affairs made it quite easy to examine the annular portion of the pancreas as well as the duodenum above and below it. Likewise, the incomplete rotation of the colon greatly simplified the subsequent operative procedure since the colon was out of the way and did not enter into the local operative field.
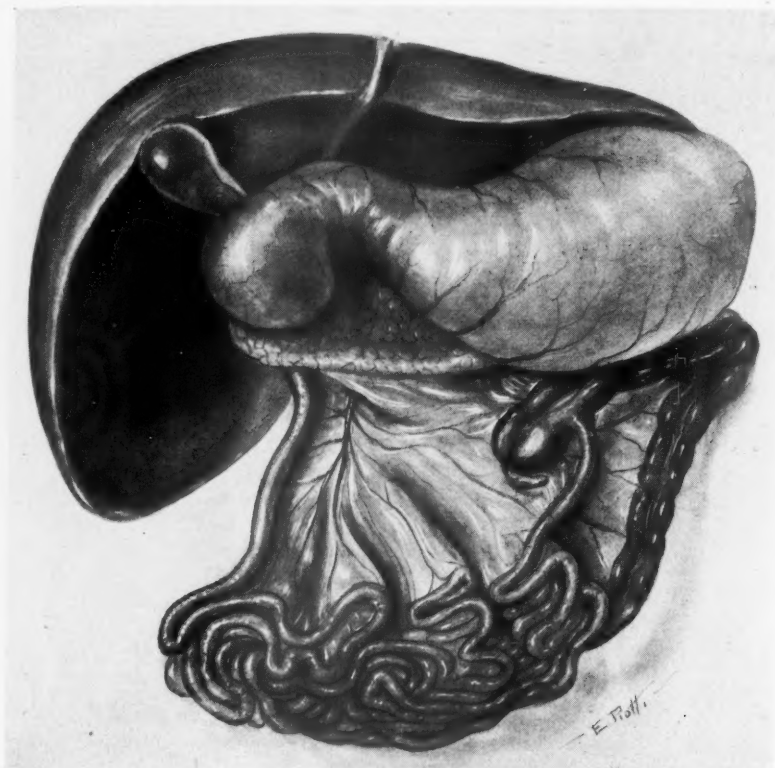

FIG. 2.—Drawing of anatomic abnormalities found at surgical exploration. Continuous with the body and head of the pancreas is a ring of pancreatic substance which completely surrounds and obstructs the duodenum. First portion of duodenum is dilated. Beyond the obstruction, the intestine and colon are collapsed. The colon is incompletely rotated.

At first sight, it appeared that the logical attack on the abnormality would be to sever the ring of pancreatic substance, or to resect a portion of the same in order to free the underlying duodenum. Such a plan was rejected because there was no way of telling whether important pancreatic ducts ran through the anterior and available part of the ring. Division of such ducts might interfere with discharge of external secretions of the pancreas into the duodenum, or, indeed, a transection of such ducts might give rise to a troublesome pancreatic fistula. Furthermore, there was no assurance that severance of the pancreatic ring would necessarily allow the constricted portion of the duodenum to dilate since this latter structure might still have an intrinsic stenosis which would require vertical incision of the narrowed duodenum and transverse suture of this wound (Heineke-Mikulicz procedure). Such a plastic repair did not appear to be an inviting form of therapy because it has been our experience in the past that a direct attack on any congenital stenosis or atresia of the alimentary tract is

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seldom as satisfactory as a short-circuiting operation by a side-to-side anastomosis. It was, therefore, decided to let the local abnormality completely alone and to perform a side-to-side duodenojejunostomy. Accordingly, the jejunum was brought upward and laid against the anterior wall of the dilated first portion of the duodenum so that an isoperistaltic type of anastomosis could be established. This was completed with two layers of continuous silk (No. ooooo Deknatel) on an atraumatic needle, making a stoma about three cm. in length. When this union had been completed, gas readily passed from
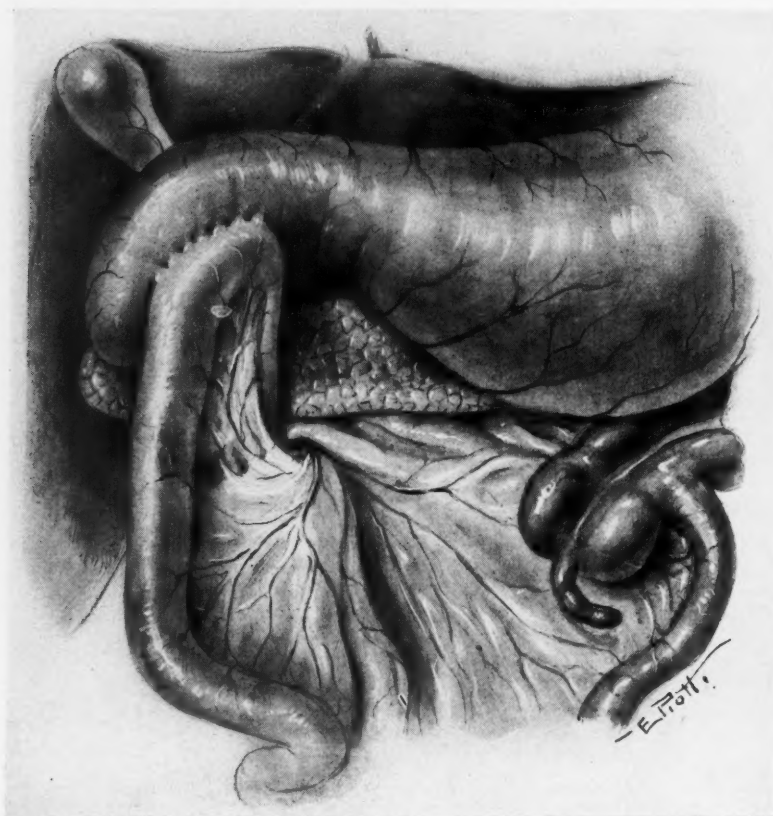
Fig. 3.—Method of surgical alleviation of duodenal obstruction by establishment of an isoperistaltic duodenojejunostomy.

the duodenum into the jejunum. Simultaneously, the first portion of the duodenum diminished to a more normal size, while the jejunum and ileum began to dilate (Fig. 3). The abdomen was closed without drainage. The peritoneum was closed with No. ooo continuous chromic catgut; all of the remaining layers were brought together with interrupted silk sutures of No. ooooo Deknatel.

Postoperatively, the patient was not placed on constant gastric suction. Instead, the stomach was lavaged every six hours for the first postoperative day. During the second postoperative day whey was offered every three hours. On the third day breast milk was given every four hours. This was increased in amount until the child was obtaining normal caloric requirements by the sixth day. Sodium sulfadiazine was given by parenteral routes for the first three days after operation. The skin sutures were removed on the sixth day and the wound healed *per primam*. The baby was discharged from the hospital

on the sixth postoperative day. There was no vomiting; she was taking her feedings well; and she was beginning to have stools which contained curds.

Subsequent development of this child has been quite normal. She has consistently taken feedings eagerly and satisfactorily; her diet has not been restricted in any way. The weight gain has been satisfactory. There have been no symptoms or signs of duodenal obstruction at any time. When last examined at 16 months of age the child weighed 23 lbs. (Fig. 4).

FIG. 4.—Photograph of patient at 16 months of age, showing satisfactory development and nutrition.

ABNORMAL ANATOMY—PATHOLOGY

In this malformation the head of the pancreas lies in its customary position in the bend of the duodenum. From this head two arms of pancreatic tissue extend around the second part of the duodenum, one anteriorly and one posteriorly. These usually fuse to form a complete encircling mass, but if a gap occurs between the two ends it is apt to appear anteriorly. Such a ring of pancreatic substance almost invariably produces, or is accompanied by, some degree of constriction in the duodenum. If this blockage is minimal, there is little or no associated evidence of intestinal obstruction. If, however, the constriction is marked, the proximal duodenum is dilated and its wall is hypertrophied. In only rare instances is there an atresia of the duodenum at the level of the pancreatic ring.

The annular portion of pancreatic substance has all of the histologic characteristics of a normal pancreas. It contains islet as well as acinar tissue. The ducts for the external secretions have been the subject of considerable investigation. They may be rudimentary and may run from the anterior part of the ring towards the left to join the main pancreatic duct. However, it is more customary for the annular part of the pancreas to be traversed by a major duct which begins anteriorly, runs to the right, and then curves around laterally and posteriorly; finally, to join either the common bile duct or the main pancreatic duct. In some of these cases the lower portion of the common duct passes through the posterior portion of the annular pancreas and is obstructed either by constriction or angulation.

The pathologic data can be divided into four general categories: (1) The changes which occur in the pancreatic substance itself; (2) the secondary effects upon the alimentary system; (3) the derangements which are sometimes found in the lower biliary passages; and, finally, (4) the associated congenital abnormalities in other portions of the body.

Numerous writers have commented upon the findings of some form of pancreatitis, either acute and hemorrhagic in nature, or chronic and cicatricial in type. Such changes may involve the main body of the pancreas, only the annular portion, or the entire pancreatic substance. Severe pancreatitis is not infrequently the illness which brings the individual to the operating table or to autopsy. The relatively high incidence of inflammatory lesions in patients with an annular pancreas certainly suggests a causal relationship to the abnormal form of the ducts. Certainly, it is conceivable that an attenuated or compressed ductal system could produce stasis and subsequent back pressure effects. Similarly, a direct communication with the common bile duct, associated with compression of the lower portion of the common duct, might lead to reflux of bile into the pancreatic system and thereby activate the pancreatic enzymes.

The secondary changes in the intestinal tract are obvious. The evidence of dilatation and thickening of the first part of the duodenum are in direct proportion to the degree of constriction which the annular pancreas produces. Gastric or duodenal ulceration has been frequently reported. This may be dependent upon stasis of gastric or intestinal contents or it may possibly be secondary to a reduced flow of pancreatic juices.

Any disturbances in the biliary system, if they occur, are purely those brought about by compression of the common bile duct as it traverses pancreatic tissue. Dilatation of the extrahepatic biliary system, stasis of bile within the liver, and evidence of icterus throughout the body may be of variable and even of marked degree. If such biliary obstruction supervenes, it is apt to be manifest in infancy or early childhood.

Finally, like any congenital malformation in the human, an annular pancreas may be associated with a considerable incidence of other anatomic abnormalities in regional or distant parts of the body. However, these are often of only academic interest and do not necessarily disturb the patient's health.

Indeed, they are frequently not suspected or discovered until exploratory celiotomy or autopsy examination. In the case herewith reported there was an incomplete rotation of the colon, which in no way interfered with the functioning of the alimentary system.

EMBRYOLOGY

Embryology of the annular pancreas has been thoroughly discussed by McNaught,[10] and others. Theoretic explanations of the anomaly are mainly twofold: Lerat,[9] Weissberg,[15] and others, contend that the annular arrangement is merely the result of hyperplasia—this is, overgrowth of pancreatic substance, dissecting in such a way beneath the serosal coat of the duodenum that it finally surrounds this part of the alimentary tube. They suggest that such an enlargement follows fetal peritonitis as a regenerative process. Most workers, however, favor the theory that the malformation results from the failure of the tip of the ventral pancreatic anlage to rotate with the duodenum —as does its ductal outlet. In consequence, a band of elongated, pancreatic tissue becomes wrapped around the duodenum in a napkin-ring fashion, and the duct from the ventral anlage sweeps around the entire duodenum to enter the duct of Wirsung.

CLINICAL DATA

In 1933, McNaught[10] reviewed the literature and collected 40 cases of annular pancreas. In 1935, he and Cox[11] presented an additional case and cited three others which had been already recorded. In 1942, Lehman[8] brought this total up to 48 cases, and particularly emphasized the clinical problem which can result from this congenital abnormality. In 1943, Chapman and Mossman[3] described the findings in a dissection room subject. This, together with our patient, now brings the number to at least 50 reports of annular pancreas in man.

Out of the above-indicated 50 examples of annular pancreas, 39 were incidental postmortem findings with little or no history of difficulty during the lives of the patients. Only 11 of the 50 subjects had complaints which led to clinical study and eventually to surgery. These are summarized in Table I. Vidal's patient, and also ours, were three days old. The age of the remaining nine varied from 26 to 74 years. It is, therefore, evident that the duodenal obstruction can be complete (Vidal's), or nearly complete (our case), so that there is evidence of duodenal obstruction in the first few days of life. Conversely, the degree of obstruction may be so slight that no complaints are referable to it until subsequent years or even adult life.

When an annular pancreas has been productive of symptoms it usually manifests itself in the form of acute or recurrent duodenal obstruction (ten of 11 cases). Hence, there may be epigastric pain, nausea, vomiting, and possibly malnutrition. The vomitus may or may not contain bile, depending upon the anatomic relationship of the common bile duct exit to the narrowed

TABLE I

CASES OF ANNULAR PANCREAS TREATED BY OPERATION

Case	Reported by	Age—Sex	Operation	Result	Remarks
1	Vidal 1905	Male 3 days	Posterior gastro-enterostomy	Cure	Also had congenital atresia of duodenum
2	dos Santos 1906	Female 26 yrs.	Posterior gastro-enterostomy	Died (pneumonia)	Had chronic interstitial pancreatitis
3	Lerat 1908	Female 46 yrs.	Resection of pancreatic ring	Cure	Drainage ceased on 13th day
4	Smetana 1928	Male 74 yrs.	Posterior gastro-enterostomy	Died	Marked fibrosis of pancreas. Ca. of cystic duct
5	Howard 1930	Female 46 yrs.	Division of ring	Cure	Pancreatic fistula, requiring second operation
6	Brines 1930	Male 35 yrs.	Drainage of pancreatitis	Died	
7	Zech 1931	Female 27 yrs.	Division of ring. Heineke-Mikulicz plastic on duodenum	Cure	Small pancreatic fistula
8	Brines 1931	Male 44 yrs.	Posterior gastro-enterostomy	Died (respiratory infection)	
9	Truelsen 1940	Male 35 yrs.	Posterior gastro-enterostomy. Plastic on duodenum	Cure	
10	Lehman 1942	Male 23 yrs.	Partial resection of ring	Recovery, but persistent symptoms	
11	Gross & Chisholm 1944	Female 3 days	Duodenojejunostomy	Cure	

portion of the duodenum. Roentgenologic examination by a barium series should give rather conclusive proof of a partial block, with dilatation of the first part of the duodenum compared to a more collapsed third part of the organ. The midduodenum is notched or constricted. Such filling defects, and associated delay in emptying of stomach and first part of the duodenum, may be indistinguishable from the picture produced by a healed duodenal ulcer which has given rise to marked duodenal deformity. However, in a subject of childhood years, such roentgenologic findings would be more suggestive of a congenital abnormality than of a peptic ulcer.

In occasional cases the symptomatology and physical findings are those resulting from acute pancreatitis. Severe abdominal pain, distention, marked tenderness, rapid pulse and rising temperature may indicate a severe and diffuse inflammation of the organ, without giving any clue regarding the underlying abnormality which probably has precipitated this condition. Indeed, operation has been performed for hemorrhagic pancreatitis and the anatomic structures have been so distorted and obscured by the inflammatory process, that the anomalous form of the pancreas was overlooked until subsequent postmortem study.

In rare instances, usually in infants dying within the first few months of life, jaundice has been the presenting complaint. It may be mild or marked. The stool contains much or little bile pigment—depending upon the degree of obstruction of the biliary passage. In one instance studied in the Children's Hospital pathology laboratory by Dr. Sidney Farber (to be subsequently reported) the common duct was completely blocked, the stools were acholic and the baby had a very high icteric index prior to its death at five months.

TREATMENT

Aside from those individuals with pancreatitis, or possibly with biliary obstruction, the necessity for operation will naturally depend upon the degree of existing duodenal obstruction and the severity of the attendant symptoms. Under rare circumstances the duodenum may be atretic (Vidal) and surgical relief is imperative in the first few days of life. Similarly, in our case, the tiny, pinhole opening representing the duodenal lumen induced a nearly-complete block and required early operative intervention. It has been more typical, however, to find that a fluid or even solid diet could be tolerated for many years before symptoms of high intestinal obstruction manifest themselves and necessitate relief.

The alleviation of duodenal obstruction could be conceivably effected in three different ways, and each type of operation has been supported by various proponents:

1. *Division of the ring of pancreatic tissue* or a resection of part of the same, has been performed by Lerat, Howard, and by Lehman. Zech followed this procedure by a Heineke-Mikulicz type of plastic enlargement of the constricted duodenal wall. All of these patients survived, but three of them developed a pancreatic fistula which gave some concern during the post-operative course. While only one of these required a secondary operation for closure of the fistula, it is well to point out that such pancreatic leakage is a distinct hazard in this type of operation. Since the pancreatic ducts may exhibit considerable variation in their distribution, the operator can never be certain when a major duct will be severed if the pancreatic ring is divided. Furthermore, simple section (or partial resection) of the ring will not always insure a complete release of the duodenum, since the latter may be constricted by intrinsic scar tissue within its wall. A review of the available cases treated by these methods leads to the distinct impression that direct attack on the pancreatic ring or constricted portion of the duodenum is inferior to a short-circuiting type of operation.

2. *A posterior gastro-enterostomy* was established by Vidal, dos Santos, Smetana, and by Brines. It was combined with a plastic repair of the duodenal wall by Truelson. Two of these patients were cured and three succumbed. This high mortality rate should not necessarily condemn the operation, since the fatalities were due to unrelated causes. Relief of the duodenal obstruction by gastro-enterostomy will probably have the largest number of adherents, since this operation is a well standardized one and will undoubtedly relieve symptoms in the majority of instances. However, it is possible that in some cases it would not effectively drain the proximal duodenum.

3. *Duodenojejunostomy* has been established in only one case—the one here reported. We believe this to be the ideal type of surgical correction, because it completely relieves the duodenal obstruction, does not interfere in any way with the gastric functions, and does not possess any of the hazards of cutting the pancreatic ring with its attendant danger of a fistula. Ladd[7]

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has repeatedly emphasized the value of duodenojejunostomy for congenital atresia or stenosis of the duodenum; such a short-circuiting type of operation seemed ideal for our patient with a duodenum obstructed by an annular pancreas. An isoperistaltic duodenojejunostomy was completed in our case with ease, in spite of the diminutive size of the distal collapsed loop of intestine. It was, of course, greatly facilitated by the congenital incomplete rotation of the colon (which made the duodenum more approachable) but the presence of a normally situated colon would not be a serious deterrent to completion of the anastomosis. After performance of this repair in our case, and being highly satisfied with the result obtained, a perusal of the literature shows that Zech, and more recently Lehman, had formerly concluded that duodenojejunostomy would be the operation of choice for these patients.

SUMMARY AND CONCLUSION

A case is reported of a newly-born infant with duodenal obstruction due to an annular pancreas. This was treated on the third day of life by a duodenojejunostomy with complete success. Pertinent facts taken from the literature regarding this congenital abnormality are briefly reviewed. The constriction of the duodenum is not always sufficient to cause clinical symptoms. If symptoms of duodenal obstruction appear, they should be relieved by surgical correction. Operative alleviation of the obstruction has been practiced by: (1) Division of the pancreatic ring—with or without a plastic procedure on the duodenal wall. (2) Posterior gastro-enterostomy. (3) Duodenojejunostomy. We believe that the first procedure is the least desirable and that the last one is the operation of choice. The case herewith described is the only one which has ever been treated by this method.

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THE CONSERVATIVE TREATMENT OF ACUTE DUODENAL FISTULA*

CASE REPORT

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A PROFUSELY DRAINING DUODENAL FISTULA is a serious and disconcerting complication of certain types of upper abdominal surgery. It carries an exceedingly high mortality rate, variously reported as from 27 to 60 per cent, or an average mortality rate including all forms of treatment of 36.0 per cent.[3] Duodenal fistulae may be classified into two main groups: (1) The lateral type, in which an opening develops in the wall of the duodenum, with the continuity of the gastro-intestinal tract intact, as follows gallbladder surgery, repair of perforated peptic ulcer, *etc.*; and (2) the end type, following the surgical closure of the amputated duodenal stump in gastric resection.[1]

The outstanding principles of therapeutics advocated in the treatment of this disease have been (1) jejunostomy and jejunal feedings, as described by McGuire and Erdman; (2) suction, as introduced by Carmen, Lahey, Potter, *etc.*; (3) neutralization of the intestinal juices as advocated by Potter; and (4) the blood chemistry changes, as demonstrated by various authors.

Acute postoperative duodenal fistulae have been reported in the literature in approximately 130 patients, and to this group we wish to add another case which made a remarkable recovery on a conservative plan of therapy.

Case Report.—Harper Hosp., No. 248275: A 64-year-old white male was admitted, March 28, 1943, with a history of gradual, painless jaundice of two months duration, clay-colored stools, weight loss and dark urine. In February, 1941, he had undergone a transurethral resection of the prostate and the removal of a diverticulum of the urinary bladder and, in July, 1942, a cholecystectomy and common duct drainage. Physical examination revealed a moderate jaundice, a slightly enlarged liver, atrophy of the small muscles of the hands, and glossitis. Laboratory data: Hb. 67.0 per cent; R.B.C. 3,620,000; W.B.C. 8,500; urine loaded with pus; blood N.C.N. 29.0 mg.; icteric index 30; and a prothrombin time of 90 per cent. *Preoperative Diagnosis:* Postoperative stricture of common duct; rule out carcinoma of the head of the pancreas.

Exploratory celiotomy, April 6, 1943, disclosed a stricture of the common duct where it passed behind the first portion of the duodenum. A longitudinal incision was made through the wall of the common duct at the stricture and closed transversely over a T-tube to enlarge the diameter of the duct. During this procedure the duodenum was torn by a Deaver retractor. It was immediately repaired with catgut and covered with a tab of omentum.

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During the third postoperative night there occurred a profuse, greenish, bile-stained and foul-smelling mucus discharge from the wound. The discharge continued to increase in amount and Wangensteen suction with a Levine tube was started in an attempt to advance the tube through the duodenum and beyond the perforation. This procedure was unsuccessful and was discontinued. The discharge macerated the skin, digested the wound, and seriously dehydrated the patient. A suction unit, of my construction, for draining sinuses was placed in the wound and all the drainage was collected before it reached the skin surface (Fig. 1). An attempt was made to refeed the secretions
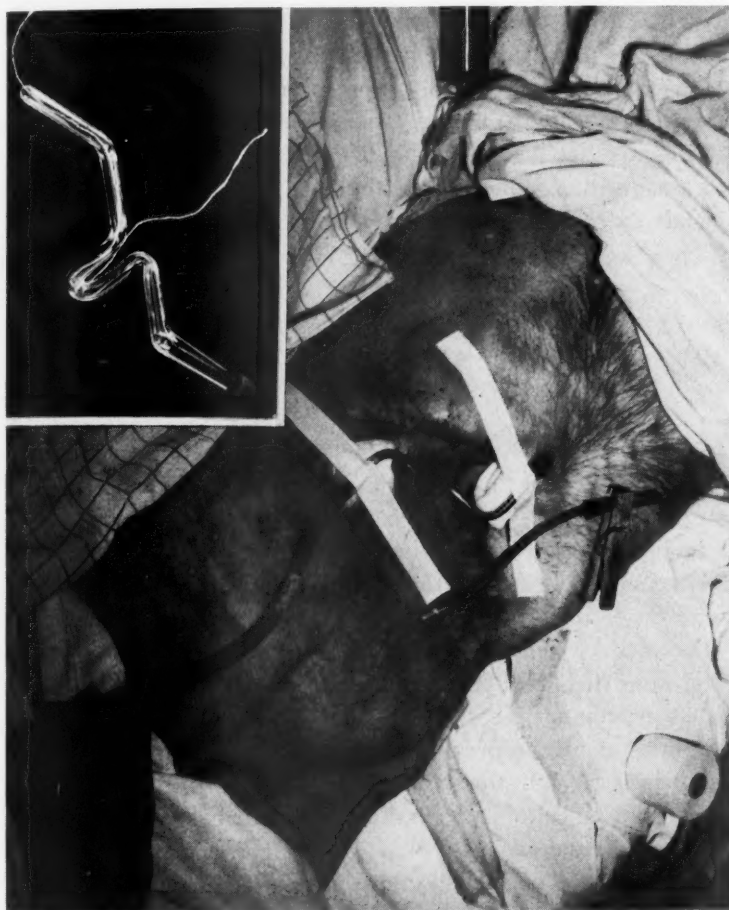
Fig. 1.—Photograph of the patient with the drainage unit inserted into the healing duodenal fistula. The jejunostomy tube is closed with a clothespin, and lies to the patient's left.

Insert.—A pyrex glass model of the drainage unit, with a piece of string entering the 'U'-arm and leaving the tube, the course of aspirated fluids. A removable rubber cap at the opposite end enables one to clean the tube easily.

or administer them in the form of retention enemata. The patient, however was entering a state of alkalosis which would soon become irreversible. On April 15, 1943, under local anesthesia, Witzel jejunostomy was established, and for the next 40 days he received the collected drainage from the fistula through this tube. On the 50th postoperative day the duodenal fistula had closed spontaneously and the jejunostomy tube was removed. On the 65th postoperative day he was discharged, completely healed.

A follow-up examination six months later found the patient looking very well, having gained 40 lbs. in weight and presenting no complaints, except a medium-sized incisional hernia for which he wears a support. There has been no jaundice, clay-colored stools or epigastric pain.

COMMENT.—The etiology of this type of lateral duodenal fistula is usually the unrecognized trauma at operation, resulting in the devitalization of the tissue followed by spontaneous perforation. Damage in our case was caused by a Deaver retractor, and the immediate repair of the rent subsequently broke down. The onset of this complication is acute and is often heralded by a state of shock, in which the patient becomes pale, cold, clammy, apprehensive and covered with beads of perspiration. The drainage from the duodenum is acrid, foul-smelling, greenish to black seromucus containing food particles and having an acid reaction.

The drainage attacks and digests the skin, resulting in a red, painful rash and ultimately extensive ulceration. The skin can be protected by an adhesive ointment made as follows:

$$\text{R}\!\!\!\!/$$

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℞  Aluminum powder...................................ounces 3
   Zinc oxide........................................ounces 6
   Petrolatum..............qs., ad..................ounces 8
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This was applied widely about the wound twice a day, and added to the comfort of the patient.

To control the fluid discharge, a metal drainage unit, a modification[4] of the McCollum tube, was inserted into the wound to collect the secretions. This unit is so constructed that continuous suction draws the secretions through the perforation on the inner angle of the U-arm and keeps the discharge from welling-up on the skin surface. The hole is protected by the arms of the U and does not become plugged with tissue from the wound edges. The total collected drainage at first amounted to 3000 cc., or more, a day, and consisted of fluids taken by mouth, gastric secretions, bile and regurgitated pancreatic juice.

The jejunostomy tube permitted the free injection of the fistulous drainage directly into the intestinal tract, where it could be best utilized by the body. Also, supplementary tube feedings of a 3000-calorie fluid diet containing 80 units of protein and adequate vitamins was administered three times a day in amounts of 6 to 8 ounces, or more, depending upon the comfort of the patient. This diet contained approximately 40 calories per ounce, and the formula was as follows:

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Milk..............................................1000 cc.
40 per cent cream................................. 400 Gm.
Eggs..............................................   6
Orange juice...................................... 300 Gm.
Lemon juice....................................... 200 Gm.
Sugar............................................. 100 Gm.
Brewers yeast.....................................   5 Gm.
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A progressive high protein diet was given the patient by mouth, beginning with a soft diet and gradually adding solid food until a full diet was reached.

The plan was to increase the viscosity of the gastric contents by utilizing the capacity of proteins to absorb water and to fix the hydrochloric acid. The more viscid the duodenal contents, the less apt they were to escape through the perforation. Secondarily, food by mouth increased the confidence and feeling of well-being of the patient.

The blood chemistry, including the nitrogen level, carbon dioxide combining power, chlorides and protein values, was carefully followed, and all parenteral therapy was given to maintain these values as close to normal as possible. The total parenteral supportive medication administered was 3000 cc. of 5 per cent glucose in saline, 4000 cc. of normal saline by clysis, 74,000 cc. of Hartmann's solution, 1500 cc. of red blood cells suspended in saline, and 4000 cc. of Amigen. Amigen was used experimentally because of its protein content but was discontinued due to the untoward side-effects of anorexia, nausea, vomiting, malaise and severe generalized headaches. During the most critical phase of the disease five units of regular insulin were administered three times a day before meals to aid carbohydrate metabolism and support the liver.

SUMMARY

(1) We have presented a case of postoperative duodenal fistula of the lateral type which drained 3000 cc., or more, a day, and recovered.

(2) A simple and efficient apparatus is described which will drain wounds and sinuses and collect the secretions in a vacuum bottle.

(3) A jejunostomy is life-saving in that it makes possible the reinjection of all the upper intestinal drainage, as well as allowing feeding directly into the intestine below the site of perforation.

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A RARE ABNORMALITY OF THE BILE DUCTS:
THE ANTEDUODENAL POSITION OF THE CYSTIC DUCT*

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Case Report.—The subject of this report was a tall, well-built, white man (E. C.) of Italian birth. He was 67 years of age, and had been in excellent health until ten years previously. At the age of 57 he began to suffer dull pain under the right costal margin, and went from one doctor to another without getting much relief.

In September, 1942, a roentgenologic examination demonstrated a nonfunctioning gallbladder and the probability that there were gallstones present. Operation was recommended but the patient preferred to wait. By May, 1943, the pain had increased in severity. The patient had lost 25 pounds, and had developed a slight jaundice. It seemed probable that a stone had moved down causing a partial obstruction of the common duct. At this time the patient requested surgical treatment.

Operation.—May 31, 1943: Under general anesthesia (30 cc. of paraldehyde rectally, followed by nitrous oxide and oxygen), the gallbladder was exposed. It was large, thickened and tense, and bile could not be expressed out of it readily, but no stones could be felt; there were several large, soft lymph nodes along the neck of the gallbladder.

The diagnosis of cholecystitis without stones was made, and cholecystectomy was begun at the fundus. Soon after starting the procedure it was noticed that the cystic duct passed *in front* of the duodenum. All the tape-sponges were removed in order to verify this anatomic abnormality. A cholecystectomy was then completed by freeing the fundus and the neck of the gallbladder in front of the duodenum, where the cystic duct was ligated at a point anterior and inferior to the duodenum at the junction of its first and second parts. By going through the hepatoduodenal omentum the hepatic duct was exposed; it was soft and not distended, but seemed to be somewhat displaced medially. Through the foramen of Winslow, one could feel the common duct, which was soft and contained no stones. While we were considering whether to mobilize the duodenum laterally or follow the stump of the cystic duct in front, in order to expose the common duct, a round, firm mass, the size of a hazel nut, was felt bulging from below into the first part of the duodenum, about one-half inch from the pylorus.

It was thought this might be an adenoma of an aberrant lobe of the pancreas which might have caused pressure on the common duct (especially if such a duct was displaced medially) and that this anomaly might account for the jaundice. It was decided to remove the tumor by the transduodenal route. A transverse incision was made across the first part of the duodenum about half an inch from the pylorus and the tumor was shelled out easily. A probe introduced into the bed of the tumor did not enter the stomach or the duodenum, showing that the mucosa was intact. When it was pushed to the right, however, a gush of thin, clear yellow bile came from under the second portion of the duodenum, indicating that the common duct was patent.

The incision in the wall of the duodenum was sutured with two rows of chromic catgut and a cigarette drain was left against the stump of the cystic duct, and the abdomen closed.

Postoperative Course.—The patient had a stormy convalescence at first. For 12 days the major part of the bile drained, probably from the duodenal suture, through the
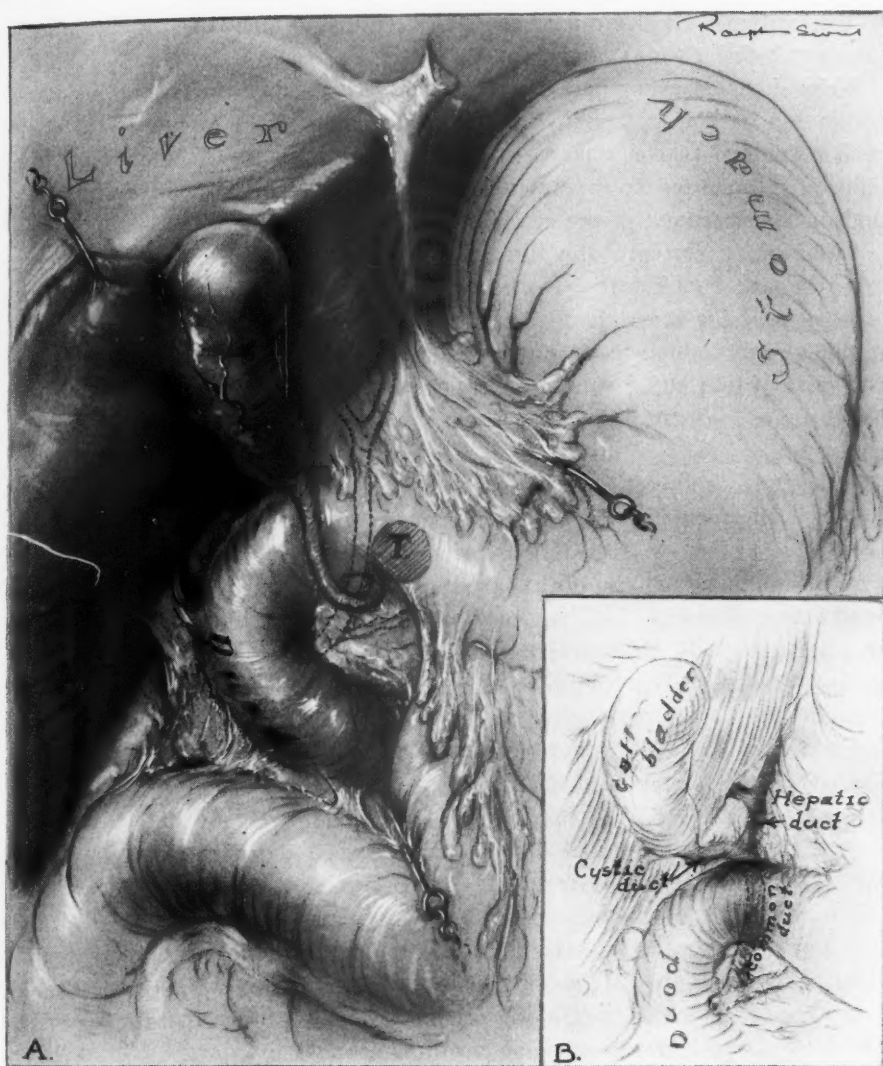

PLATE I.—A. Drawing showing abnormality of the cystic duct, and the site of the tumor, as observed at operation.

B. Insert showing comparative appearance of the normal anatomic relations.

abdominal incision. After that the flow of bile decreased rapidly, and three weeks after operation, the abdominal incision was well healed, the biliary fistula having closed entirely. The patient had no more jaundice, his appetite was good, and his weight was 167 pounds.

Pathologic Report: Typical duct carcinoma arising from the bile duct.

A consultation was requested because of the pathologic diagnosis. The question of more radical intervention was discussed and was explained in detail to the family. They decided in favor of a "Whipple operation." This was performed elsewhere. The patient succumbed to shock on the third day. The surgeon in the case told me that he found "shreds" of cancer in the head of the pancreas. Autopsy was refused.

Two authors who have paid especial attention to anomalies of the biliary ducts are Kehr[1] (1913), and Gross[2] (1936).

Kehr sketched every possible abnormality of the bile ducts, but he made no mention of any instance of an anteduodenal position of the cystic duct. Gross's comprehensive report, containing 148 cases of anomalies of the gallbladder, collected from the literature, failed, also, to mention an anteduodenal displacement of the cystic duct.

Embryology can probably throw some light on this unusual anomaly. From the text books dealing with the development of the abdominal organs we learn that the liver "bud" starts from a ventral diverticulum appearing on the foregut (duodenum) in the first weeks of intra-uterine life. The distal part of that bud forms the liver, while the proximal part of the original diverticulum constitutes the bile ducts of which the gallbladder is just an evagination.

In normal subjects, when the gallbladder "bud" appears, a certain time after the formation of the liver bud, the cystic duct joins the common duct at two-thirds or three-fourths of the distance from the surface of the liver to the duodenum and always passes *behind* this portion of the intestine. Should the gallbladder "bud" appear very early after the liver bud has formed, the gallbladder will be found very near the liver, or it may even be "completely intrahepatic," a condition of which Gross found four instances mentioned in the literature.

Failure of the gallbladder "bud" to appear altogether results in total absence of the gallbladder. Gross listed 38 such occurrences from the literature.

The case herewith reported would lie between those two extremes; the gallbladder bud probably started to grow late and at the time when the rotation of the stomach and duodenum to the right had been completed and these viscera had already become firmly attached to the vertebral column; by this disposition, the gallbladder bud, appearing too late, would be prevented from expanding behind the duodenum but would be deflected forward and forced to assume an anteduodenal position.

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TREATMENT OF HORSESHOE KIDNEYS

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REFINEMENTS in operative technics have resulted in increasing interest in congenital anomalies of the genito-urinary tract. During recent years a voluminous literature has accumulated concerning the various types of renal fusion, especially the so-called "horseshoe kidney." Morgani presented the first accurate description of this anomaly in 1820, although it was mentioned by Berengari da Carpi as early as 1522. In 1934, Gutiérrez correlated the many features of horseshoe kidney in his monograph and established it as a distinct clinical entity capable of producing bizarre symptom complexes.

The purposes of this report are: (1) To remind practitioners of the incidence and significance of horseshoe kidneys; (2) to review the accepted forms of surgical treatment; and (3) to add a case to the very small group which has been treated successfully by symphysiotomy and bilateral nephropexy.

When the renal blastemae or anlagen fuse along their mesial borders instead of remaining separate, the resultant anomaly is classified as one of median fusion. The horseshoe kidney represents the most common type of such anomalies and has been observed in embryos 30 Mm. long. In 90 per cent of the cases this fusion occurs at the lower poles while in the remaining 10 per cent the upper poles are joined. The isthmus may be merely a thin fibrous cord, a tenuous membrane, or a thick mass of renal tissue containing glomeruli and tubules. This isthmus usually passes anterior to the aorta and vena cava. Four cases have been reported in which the isthmus was dorsal to the great vessels and in one reported instance the isthmus passed *between* the aorta and vena cava. According to Eisendrath and Rolnick, the most common level for the isthmus is at or close to the aortic bifurcation.

Variations in the origin, number and size of the renal vessels are encountered frequently. The isthmus may have what appears to be a separate blood supply. The sympathetic nerve plexuses and the ureters usually cross the anterior surface but specimens have been reported in which the ureters were dorsal to the isthmus.

Normal rotation of the kidneys is prevented by the fusion and the resulting displacement of the pelves forms the basis for pyelographic diagnosis. In some instances the soft tissue shadows of the kidney demonstrate the horseshoe shape of the parenchyma. Occasionally the isthmus may be outlined distinctly in plain roentgenograms. Some examiners have been able to palpate thick zones of fusion in thin patients. The diagnosis of horseshoe kidney usually is made by the pyelographic evidence of inversion and rotation of the renal

pelves, unusual localization of the elongated and bizarrely-shaped pelves and peculiar position of the ureters.

Foley has summarized the roentgenologic findings typical of horseshoe kidney as: (1) Low position of the kidneys; (2) inferior calices extending dorsally or medially from the pelvis; (3) ureteropelvic junction on the ventral surface instead of at the medial border of the pelvis; (4) ureter overlying the pelvis and crossing the abnormally directed inferior calices; and (5) long axis of the kidney oblique toward the midline below.

Horseshoe kidneys have been classified in a variety of ways but these groupings embody the following distinctions:

    I. No renal pathology except the fusion and no symptoms.

    II. Pathologic conditions superimposed on the anomaly, with or without symptoms.

    III. No secondary renal pathology but definite symptoms referrable to the fusion *per se*.

I. HORSESHOE KIDNEY ALONE, WITHOUT SYMPTOMS

The anomalies of this group are discovered incidental to some other clinical study or are noted during postmortem examinations. The autopsy incidence of horseshoe kidney indicates that this is by far the largest group of such cases. Statistics vary from the 1:385 reported by Shoemaker and Braasch to the ratio of 1:1000 noted by Davidsohn, as shown in Table I.

TABLE I

INCIDENCE OF HORSESHOE KIDNEY DISCOVERED AT AUTOPSY

Authors	Ratio
Shoemaker and Braasch	1:385
Papin	1:500
Lipschutz and Hoffman	1:576
Naumann	1:600
Lowsley and Kirwin	1:600
Jeck	1:643
Thompson	1:678
Motzfield	1:710
Boetz	1:715
Carlier and Girard	1:862
Davidsohn	1:1000

From these statistics it is obvious that most horseshoe kidneys are not recognized clinically. Although many of these patients undoubtedly have no symptoms to direct attention to the anomaly, some patients may belong in Group III because of vague abdominal complaints which are not diagnosed properly or for which the patient does not seek relief.

Urologists are agreed that patients with asymptomatic horseshoe kidneys and no secondary renal pathology should not be subjected to operation because of the anomaly alone. There can be no question that the lives of patients in this group are not jeopardized by further observation.

II. SECONDARY RENAL PATHOLOGY. WITH OR WITHOUT SYMPTOMS

From the many case reports in the literature it is apparent that this group represents the next most common type of horseshoe kidney. Many writers insist that secondary pathologic processes tend to develop more frequently in anomalous kidneys than in normally formed organs. Recent evidence by some investigators adds support to this contention even though the subject remains controversial.

Almost every known type of pathology has been found in horseshoe kidneys. DeVries reported a case in which one-half contained a calculus, a papilloma and a hypernephroma. Joly claims that calculi occur six times more frequently in horseshoe kidneys than in normal ones. Walters and Priestley reported 68 cases of horseshoe kidney, verified at operation, and only seven had no secondary pathology. Rathbun reviewed 108 cases and reported calculi in 32, hydronephrosis in 18, tuberculosis in 12, and pyonephrosis in 11.

The symptoms in such cases are those characteristic of the secondary diseases in most instances. Occasionally these complaints are combined with those typical of the "horseshoe kidney syndrome" which will be considered in the next group. Not infrequently, however, the secondary pathology in horseshoe kidneys is discovered accidentally in the course of routine examinations just as such conditions some times are found in normally formed kidneys. These asymptomatic patients may require radical therapy because of the gravity of the secondary pathology (*e.g.*, hypernephroma, without clinical symptoms).

Braun has been credited with the first attempt to remove the diseased half of a horseshoe kidney in 1882, without success. Six years later Socin removed the hydronephrotic half in two stages, and the patient lived. Since then there have been many case reports of partial removal of horseshoe kidneys and other types of surgery performed because of secondary pathology. In 1928, Lowsley and Kirwin collected 92 cases of heminephrectomy. Eisendrath and Rolnick mention 250 operated cases and list the following procedures; Primary heminephrectomy, 117, pyelotomy and nephrotomy, 70, secondary heminephrectomy, 13, combined pyelotomy, symphysiotomy and nephropexy, 17, pyeloplasties or ureterolyses, 3, various procedures employed in injuries to horseshoe kidneys, 9.

Goldstein and Abeshouse (1943) reported four cases in which the operative procedures were limited to heminephrectomy and pyelolithotomy. From their study they concluded that "horseshoe kidneys that are exposed because of renal disease should have hemisection after the pathologic process has been corrected, horseshoe kidneys with small calculi in the calices should be heminephrectomized, horseshoe kidneys causing pain or other symptoms without renal disease should be sectioned."

It is generally agreed that pathology in either half of a horseshoe kidney should be treated the same as similar lesions in nonfused kidneys. If removal

of the diseased part is indicated, heminephrectomy is the procedure of choice. If less radical treatment seems necessary (*e.g.*, pyelolithotomy), the isthmus of fusion should be divided and nephropexy performed for reasons to be explained in the following group. The consensus of opinion is that extraperitoneal approach through the usual lumbar incision should be employed for all such operations.

III. NO SECONDARY PATHOLOGY, BUT VAGUE SYMPTOMS

Horseshoe kidneys without additional pathologic changes are now recognized as being capable of producing symptoms which can be cured only by operation. Gutiérrez maintains that continuous pressure exerted upon the pre-isthmial nerve fibers by the abdominal viscera and upon the underlying mesenteric plexus and lumbar sympathetic nerves by the isthmus is the chief factor in producing the abdominal pain of the horseshoe kidney syndrome.

Rovsing has been credited with first describing the syndrome encountered in this group. This is characterized chiefly by pain in the upper abdomen, produced or aggravated by ventral extension of the spine. It may vary greatly in intensity and at times may simulate the crises noted in tabes dorsalis but usually is dull and relatively mild.

Gutiérrez has outlined the horseshoe kidney syndrome as (1) urologic symptoms; (2) indefinite renal or abdominal pain; and (3) reflex symptoms manifested by gastro-intestinal disorders.

Foley claims that the pain present in his series of seven patients was fairly typical of renal origin.

Lowsley and Kirwin explain that 12 patients observed at the New York Hospital with horseshoe kidneys had been operated upon for relief of symptoms which had been diagnosed erroneously as chronic appendicitis, cholecystitis, cholelithiasis and other intra-abdominal conditions which were not connected with the genito-urinary tract.

Martinow performed the first symphysiotomy for horseshoe kidney in 1910, and used a transperitoneal approach. Papin, in 1922, performed the first successful division of the isthmus through an extraperitoneal exposure. Donohue, in 1932, reported the first such extraperitoneal operation in this country.

Baker and Colston found only 24 cases treated by symphysiotomy in the literature prior to 1936. Seventeen of these were from Europe. They added two of their own cases to this group.

Strode was unable to find any additional cases treated by symphysiotomy in the literature from 1936 to 1939 but reported his case in which symphysiotomy and nephropexy were performed, followed one year later by nephropexy on the opposite side.

In 1940, Foley collected only 19 authentic cases of symphysiotomy and nephropexy from the accumulated literature and added seven such cases which had been under his observation. This group included the case

reported previously by Donohue, one unilateral fused kidney and five new cases of horseshoe kidney. Because of pain which persisted after the unilateral nephropexy, Foley found it necessary to perform a nephropexy on the opposite side in four of his patients. In all four instances, fixation of both halves resulted in disappearance of all symptoms. Of the total 26 patients in the literature who had been treated by symphysiotomy and nephropexy and reviewed by Foley, 92 per cent had excellent or good results and only one operative death resulted.

Goldstein and Abeshouse suggest that "cases without definite renal pathologic changes but presenting symptoms either of renal or other origin should certainly receive the benefit of surgery by performing symphysiotomy and nephropexy. We are certain that failures are going to be reported. In view of the fact that something must be done about these cases they should be given the benefit of the doubt."

In light of these observations, it seems reasonable to conclude that any uncomplicated horseshoe kidney with this symptom complex should be subjected to symphysiotomy and nephropexy in the absence of other explanatory pathology and nephropexy should be performed on the opposite side if these symptoms persist.

The extraperitoneal lumbar approach is recognized as the exposure of choice for this group.

Because of (1) the interesting and confusing symptomatology; (2) the extreme paucity of symphysiotomy reports in the literature; (3) the need of bilateral nephropexy in this instance; (4) the successful nonoperative treatment of postoperative calculi; and (5) the excellent end-result, the following case is added to the very small list of such patients who have been treated by these methods. This represents the only horseshoe kidney found at this hospital in 747 patients studied pyelographically during the 12 months from September 1, 1942, to August 31, 1943.

CASE REPORT

The patient, a 28-year-old white male, was admitted on the Medical Service, November 3, 1942, complaining of upper abdominal and left flank pain. For two years he had had frequent, dull, nonradiating, epigastric pain aggravated by lying flat on his back. This was unrelated to meals. There had been no nausea, vomiting or urinary symptoms. At no time was the discomfort severe enough to alter his general activity and relief was obtained usually by erect position. On the day of admission he began to have dull, nonradiating pain in the left flank for the first time.

Physical examination was negative except for slight tenderness just above the umbilicus and in the left costovertebral angle. There were no palpable masses. Blood pressure 118/70.

The urine showed specific gravity 1.025, no albumen or sugar, occasional W.B.C. per H.P.F., and was sterile on culture. Blood studies revealed R.B.C. 4,670,000, Hb. 90 per cent; W.B.C. 9100; sedimentation rate 2 Mm. in one hour; negative Kahn; clotting time 5 minutes; bleeding time 4 minutes, N.P.N. 30.2 mg. per cent.

Roentgenograms of the esophagus and stomach were normal but the duodenal bulb showed some irritation. This subsided on antispasmodics, but the original complaints
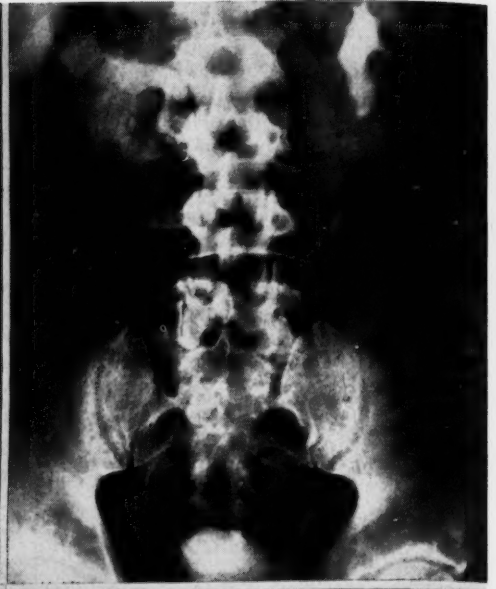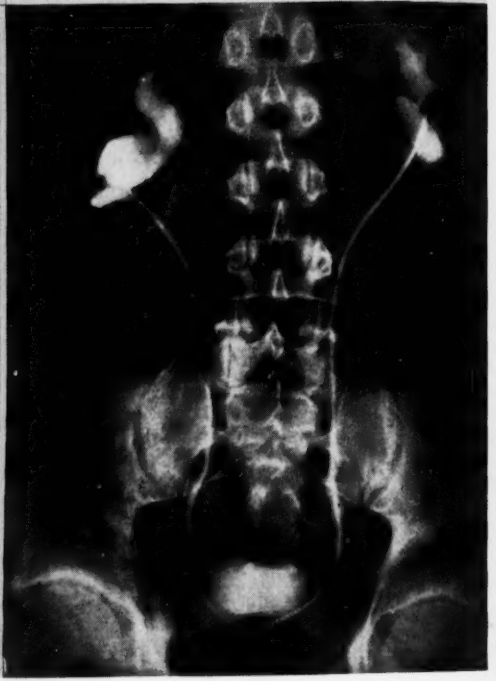
Fig. 1

Fig. 2

Fig. 3

Fig. 4

persisted unchanged. Subsequent plain films of the abdomen showed two opacities in the region of the left kidney (Fig. 1). An intravenous urogram showed these to be included in the left renal pelvis; normal function on both sides; incomplete rotation of both pelves; the right ureter deflected to the left and the right pelvis almost in the midline (Fig. 2). Cystoscopy revealed a normal lower urinary tract and retrograde pyelograms presented essentially the same renal picture as noted on excretion urography. The kidney shadows were seen to extend towards the midline with the lower poles apparently continuous.

A diagnosis was made of horseshoe kidney with calculi in the left half. The patient was transferred to urology and, on November 17, 1942, the left half of the kidney was explored, under nitrous oxide-ether anesthesia, through a flank incision.

The left half of the kidney was elongated, the pelvis and ureter were on the anterior surface and at the lower pole was an isthmus of fusion 3 cm. wide and 1.5 cm. thick. Within the pelvis could be felt the larger of the calculi. The isthmus was divided between two rows of No. 1 chromic catgut mattress sutures, after which the kidney was delivered easily, the pelvis opened, the calculi removed, and the pyelotomy wound closed with continuous No. 0000 chromic catgut, without drainage. The posterior surface of the kidney was sutured to the deep lumbar muscles with No. 1 chromic catgut after rotating the lower pole laterally to assume a more normal position. The renal fossa was drained and the incision was closed in layers with No. 1 chromic catgut in the muscles and fascia and silk in the skin.

The convalescence was entirely uneventful. The incision healed promptly. The left flank pain disappeared entirely but the epigastric discomfort persisted, although the latter was not severe. Postoperative roentgenograms showed no remaining calculi, the left kidney in much better position, with no suggestion of hydronephrosis and the right kidney still occupying the position over the great vessels (Fig. 3).

The patient was discharged December 24, 1942. He continued to have the epigastric discomfort at irregular intervals and was readmitted March 20, 1943. Examination showed no tenderness or weakness on the left side, localized tenderness near the midline just above the umbilicus and was otherwise negative. All laboratory studies, again, were negative and the urine had remained sterile. Further roentgenologic studies showed no appreciable change from the last examination (Fig. 3). The persistent complaints were thought to be due entirely to the abnormal position of the right kidney.

On March 25, 1943, the right kidney was exposed extraperitoneally through a flank incision under nitrous oxide-ether anesthesia. This half of the original horseshoe kidney also was elongated. The ureter was grossly normal and joined the pelvis on the anterior surface of the kidney with no demonstrable obstruction. After freeing the upper portion of the kidney, the isthmus was exposed, freed easily from the vena cava but was found to be adherent at the site of the previous division overlying the aorta. A large artery and vein supplied the isthmus in the midportion and after ligating and dividing these vessels, the tissue of the isthmus promptly changed color. Further division of the isthmus near the preaortic adhesions resulted in no bleeding and permitted free delivery of the kidney.

The discoloration of the isthmus extended to the lower pole of the kidney. This

FIG. 1.—Plain roentgenogram showing two calculi in region of left renal pelvis.
(*Photograph by Signal Corps, U. S. Army*)

FIG. 2.—Preoperative intravenous urogram showing good function, incomplete rotation, kidneys near midline (especially right), and soft tissue shadow of right kidney extending to vertebrae inferiorly.
(*Photograph by Signal Corps, U. S. Army*)

FIG. 3.—Intravenous urogram after symphysiotomy, left pyelolithotomy and left nephropexy showing left kidney in more normal position, no hydronephrosis and right kidney still near midline.
(*Photograph by Signal Corps, U. S. Army*)

FIG. 4.—Retrograde pyelograms after right nephropexy showing both kidneys and ureters in relatively normal position without hydronephrosis.
(*Photograph by Signal Corps, U. S. Army*)

wedge of tissue was excised and the lower pole of the cortex was closed with No. 1 chromic catgut over fat. The kidney was rotated into the space just below the diaphragm and fixed with three No. 1 chromic catgut sutures which had been placed beneath the true capsule on the posterior surface and brought out through the full-thickness of the lumbar muscles. One Penrose drain was left in the wound and the incision was closed in layers.

The wound remained dry and the Penrose drain was removed after 48 hours. The

FIG. 5   FIG. 6

FIG. 5.—Plain roentgenogram five weeks after second operation showing new calculi in both renal areas and in lower segment of left ureter.
(*Photograph by Signal Corps, U. S. Army*)

FIG. 6.—Plain roentgenogram after repeated lavage with Suby's solution "G" showing disappearance of shadows noted in Figure 5.
(*Photograph by Signal Corps, U. S. Army*)

incision healed *per primam. The epigastric pain disappeared entirely.* A plain roentgenogram and pyelographic studies on the twentieth postoperative day showed no calculi, no change in the left kidney and the right kidney in much better position with no hydronephrosis (Fig. 4). The patient was ready to leave the hospital when, suddenly, on April 26, 1943 (32 days postoperative) he began to have sharp pain in the left flank radiating to the left side of the scrotum. Further roentgenograms showed calcification in both renal areas and in the left ureter (Fig. 5). From the available cystoscopic and radiographic evidence it was assumed that these calculi had developed rapidly and probably were comparatively soft. Blood calcium and phosphorus determinations were within normal limits.

During the following three weeks the patient was cystoscoped, indwelling bilateral ureteral catheters were inserted for 48 to 72 hours on six occasions, and the renal pelves were lavaged with Suby's solution "G" (citric acid 32.3 Gm., magnesium oxide 3.8 Gm.,

sodium carbonate 4.4 Gm., distilled water ad 1000 cc.) at intervals of one to three hours. Small doses of sulfathiazole were given during this period of frequent instrumentation. The ureteral calculi passed spontaneously. The calcification in both renal pelves disappeared (Fig. 6). The patient remained asymptomatic and left the hospital, June 1, 1943, with sterile urine.

Follow-up studies have been frequent and have failed to show any recurrence of the calculi. The patient has remained asymptomatic. Pyelographic study, September 21, 1943, failed to show any change from that demonstrated after the second operation (Fig. 4). The patient was seen last September 21, 1943, but correspondence of December 15, 1943, reveals that he is still entirely asymptomatic.

Résumé: This patient with a horseshoe kidney had epigastric symptoms more or less typical of the classical syndrome and was treated for pyloric spasm (which had been demonstrated roentgenologically) without success. Relief was obtained only after symphysiotomy and bilateral nephropexy. Despite the chronicity of the symptoms due to the anomaly *per se*, he did not seek treatment until calculi had formed in the left half of the kidney and had become symptomatic. If these calculi had not been demonstrated in a routine plain roentgenogram, attention might never have been directed to the urinary tract and the fundamental pathology might have gone unrecognized. Although removal of the calculi and fixation of that kidney promptly eliminated the left renal complaints, the more classical symptoms persisted because the right kidney was situated over the great vessels. These in turn stopped as soon as the deformity was corrected. Even though this patient had no postoperative hydronephrosis and the urine remained sterile, calculi developed in both kidneys after the operation on the right. These were dissolved or passed spontaneously as fragments after frequent irrigation with Suby's solution "G" through indwelling ureteral catheters. The fact that the recurrent calcification was recognized early may have enhanced the response to this nonoperative treatment of the stones. The patient has remained asymptomatic and has had no further recurrences during the subsequent seven months.

SUMMARY

The incidence of horseshoe kidney is approximately 1:600 in clinical and postmortem examinations. Most of these are discovered accidentally, have no secondary renal pathology, produce no symptoms and require no treatment.

Not infrequently, secondary lesions develop in horseshoe kidneys and may be of any of the pathologic types which affect the nonfused kidney. These cases represent the most common type of symptomatic horseshoe kidneys which are recognized clinically and the symptoms usually are due to the secondary pathologic processes. Secondary disease of major significance should be treated by heminephrectomy. Less radical procedures which preserve both halves of the kidney (*e.g.*, pyelolithotomy) should be accom-

panied by symphysiotomy and nephropexy on that side because of the danger of remaining symptoms attributable to the fusion alone.

A small but distinct group of horseshoe kidneys without secondary pathology will present vague abdominal or back symptoms which may be mistaken for gastro-intestinal disorders or pathology in some other system. Apparently the symptoms of the "horseshoe kidney syndrome" are produced by pressure on adjoining nerves by the isthmus of fusion or by the ectopic renal masses. Relief is obtained by symphysiotomy and nephropexy. In a few such cases it may be necessary to perform a nephropexy on the opposite side also before *complete* relief is obtained.

In all surgery on horseshoe kidneys the conventional, extraperitoneal, lumbar approach is satisfactory and the one of choice.

Another case is added to the small list of patients treated successfully by symphysiotomy and bilateral nephropexy. Pyelolithotomy also was performed in this case. Recurrent calculi were recognized early and dissolved with Suby's solution "G" after irrigating the renal pelves through indwelling ureteral catheters. The patient has been followed for seven months with no further recurrence of calculi or symptoms.

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WILMS' TUMOR IN A HORSESHOE KIDNEY*

CASE REPORT

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THIS CASE is presented because it combines an unusual lesion with several problems in clinical management.

CASE REPORT

The patient, a child, age six, was admitted to the University of Pennsylvania Hospital in November, 1943, with a large abdominal tumor and high fever. She had apparently been well until the age of two and a half years, when she had the first of a long series of unexplained febrile illnesses usually ascribed to upper respiratory infections and bronchitis. During one of these episodes she was studied in another institution and found to have what was thought to be an enlarged spleen. No definite diagnosis was made and the child disappeared from medical observation until shortly before the present hospitalization. On admission, she appeared acutely ill with a high, spiking temperature ranging between 101° and 104° F. A large, smooth, rounded mass occupied almost the entire left side of her abdomen. Tympany over the mass suggested that it was retroperitoneal and not of splenic origin. Blood pressure 140/94. Blood urea nitrogen—normal. Repeated uranalyses were normal. Blood studies showed normal values except for a mild leukocytosis.

An intravenous urogram showed a horseshoe kidney in an ectopic position, with the right component overlying the sacrum and the left lying just above the pelvic brim. There was good clearance of dye bilaterally.

A large soft tissue mass containing calcium was situated in the left upper quadrant above the renal area. The iliopsoas shadow on the left was obliterated in addition to the transverse process of the 12th dorsal vertebra.

Barium enema showed an intrinsically normal colon displaced forward by the mass. Chest roentgenograms and complete bone survey were negative.

Operation.—The child was operated upon November 19, 1943, through a transperitoneal approach and a tumor found arising from the upper pole of the left segment of a horseshoe kidney. The lesion, including the entire left renal component, was removed without difficulty; dividing the horseshoe at its symphysis. There was no evidence of any metastatic spread. The tumor was apparently completely removed. The child's postoperative convalescence was entirely uneventful. Her fever disappeared and she was discharged two weeks later with a normal urine, blood urea nitrogen and urinary output. Since discharge she has remained well, gaining almost 15 pounds in two months.

Pathologic Examination.—The microscopic sections showed the lesion to be an embryoma of the kidney containing both carcinomatous and sarcomatous elements. There was no evidence of infiltration in the small margin of normal kidney removed with the tumor. *Gross Description:* The specimen consists of a rounded encapsulated mass 15 x 10 x 48 cm. and a small piece of tissue apparently kidney measuring 5 x 3 x 2 cm. The large mass is grey and shows some nodularity and on cut surface it bulges. It is quite soft. When cut, the surface is not homogeneous but apparently composed of several elements. The greater part is a yellow-grey, very soft lobular tissue in the center of which are strands of yellow and yellow-green tissue. This is slightly more firm. At one

pole there is a small hemorrhagic cystic area about 2 cm. in diameter. Sections are taken from several areas of the tumor. The small specimen shows on one side apparently normal pink tissue from kidney and on the other side greyish tissue but fairly firm. Sections are taken across this at three points and parallel to the grey surface. These are labelled A. Calcified plaques are palpable beneath the capsule. Fixation—Bouin's. *Microscopically*, the specimen shows large areas of low columnar cells which have quite large nuclei. These are arranged in a glandular fashion in some places but in many other areas they seem to be wildly growing with no tendency toward acini formation. Some acini shows a tendency toward cyst formation. There are many necrotic areas in the tumor and some areas of hemorrhage. There are some fibrous tissue septa through the tumor, some of which have a myxomatous appearance. The small piece of kidney shows no evidence of infiltration of tumor in any area. No smooth muscle elements are found. *Pathologic Diagnosis:* Embryonal sarcoma of kidney (adenosarcoma type). *Note:* This tumor apparently belongs with adenosarcoma sub-classification of the Wilms' tumor group although the glandular differentiation predominates. The resection is wide of the tumor.

DISCUSSION

The problems presented by this case are: First, the best treatment of a Wilms' tumor; and, second, the problem of treating a Wilms' tumor in one segment of a horseshoe kidney. Although embryomas of the kidney are one of the most common tumors of the abdomen in childhood, rarely have these children lived to reach puberty. It has been stated that in a series of 500 tumors of all types in children, 20 per cent were kidney tumors. Practically all of these were embryomas. Considerable pessimism has sprung up regarding the prognosis for children with this tumor, and while it is still true that the toll is high, the outlook is not as hopeless as many would suggest. A review of Ladd's statistics for the Children's Hospital in Boston indicates that about 25 per cent of his cases have survived long enough to be considered cured.

In the treatment of these tumors there are two schools of thought. The first, and older group, advocates preoperative irradiation over the growth with two objects in mind: (1) To reduce the size of the local mass so that it will be technically easier to remove; and (2) to kill off the more malignant, radiosensitive cells in the tumor and thus prevent their escape into the blood stream during the operative manipulation.

Again, Ladd, with probably the greatest personal experience with the problem at the present time, recommends removal of the mass as soon as discovered using the transperitoneal approach with ligation of the renal vessels before manipulation of the mass. He is convinced that roentgeno-therapy has been too widely employed without consideration of the end-results obtained. Perhaps the most convincing arguments in favor of his thesis are the reputed cures. The few apparently cured patients referred to in the literature received no preoperative irradiation.

During the last eight years Ladd has removed 22 Wilms' tumors, with no operative mortality, thus refuting the statement that preoperative irradiation is necessary to obtain a low operative mortality.

Listed in his series as probable cures of renal embryomas are 14 out of

56 cases alive and well from two to 21 years after operation. Only one of those 14 patients had preoperative irradiation.

Bothe, in an analysis of 44 cases from the literature, found that recurrences and metastases were reported in some cases ten years after the removal of the primary growth. With this possibility in mind he states that the most skeptical analyst would accept but eight of the 44 as cured. It is important to note that the eight cases of probable cures never had either pre- or postoperative irradiation. He personally adds seven cases treated without irradiation, and finally states that he agrees with Ladd in voicing the opinion that in these mixed tumors or embryomata immediate removal gives a better chance of cure than does irradiation and a delayed nephrectomy.

Finally, the case of the complicating problem of a horseshoe kidney must be considered. This, in itself, is not a particularly uncommon anomaly. It is associated with a high percentage of pathologic lesions mostly dependent on the high ventral implantation of the ureters, a situation resulting in poor drainage from the renal pelvis. There are few recorded instances of renal tumors associated with horseshoe kidneys. Fortunately, this tumor was isolated in the upper pole of one segment and the remaining tissue appeared normal and uninvolved.

Gutiérrez speaks of the "horseshoe kidney disease" stating that these kidneys almost invariably, sooner or later, develop nephritis, pyelitis, pyonephrosis or stone, with resultant death. They are not immune to hypernephroma and papillary carcinoma but rarely produce the Wilms' lesion. In fact, we could not find a single case of the latter reported in the literature.

This anomaly is usually the results of lower pole union, seldom of upper pole union, so often accompanied by other anomalies, such as horseshoe suprarenals, diaphragmatic hernia and spina bifida. Of great importance is the anomalous blood supply of this double kidney. The arteries usually enter the kidney posterior to the pelvis and vary in number from four to as high as six with one or two entering the symphysis itself. The ureters cross in front of the symphysis and anomalous or aberrant arteries are the rule, often taking their origin from the arteries of adjacent structures. These conditions must, of necessity, jeopardize a successful transplantation of the reconstructed nephros.

The question of further care for this child now remains. Roentgenotherapy has been decided against because she has no known malignancy remaining in her body. If she survives a sufficiently long period of time without metastasis it would seem advisable to attempt some form of nephropexy to protect her remaining kidney from the usual obstructive and inflammatory processes resulting from the ectopic position of the organ, its ureter and pelvis.

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CRUDE PENICILLIN: ITS PREPARATION AND CLINICAL USE EXTERNALLY

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THE MANY REPORTS on the parenteral use of concentrated and purified penicillin have established its efficacy in cases of bacteremia, meningitis and internal abscesses. Florey,[1] Abraham, Chain and Fletcher,[2] and the Committee of Medical Research,[3] have also reported that the concentrated and purified penicillin has been effective when applied externally in cases of acute osteomyelitis, furuncles, soft tissue abscesses and wounds. Recently, Robinson and Wallace[4] investigated the possibility of using crude penicillin externally, as the supply of the purified product is still limited and not generally available. Filtrates of *Penicillium notatum* cultures and gauze dressings which were inoculated with the fungus were applied directly on infected wounds and abscesses. Excellent results were obtained when this treatment was continued for three to six days.

As crude penicillin seemed to be a promising therapeutic agent for localized infections, a study was undertaken at the Willard Parker Hospital to determine the efficacy of this product when applied as nose and throat drops in cases of laryngotracheal infections. Crude penicillin was available at this hospital, as it has been used since 1941 in media to isolate *H. influenzae* from mixed cultures.[5]

PREPARATION OF CRUDE FILTRATES OF PENICILLIN

The crude penicillin filtrates used were prepared by the Fleming[6] method, with a few modifications. We found that the following medium gave excellent yields of penicillin:

Tryptose-phosphate broth—Difco::::............	29.5 grams
Magnesium sulphate........................	1.0 gram
Potassium chloride.........................	1.0 gram
Sodium nitrate............................	3.0 grams
Brown sugar..............................	30.0 grams
Tap water................................	2,000 Ml.

Sterilize in autoclave for 15 minutes at 15 lbs.

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PROCEDURE

1. A fairly large inoculum of both spores and mat of a known culture of *Penicillium notatum*, obtained from the American type culture collection, was grown in shallow layers of broth. Seventy-five milliliters of this broth in 250 Ml. Erlenmeyer flasks gave the best yields of penicillin.

2. The cultures were kept at room temperature (20° C.) in the dark for eight to ten days, depending on the rate of growth. A heavy mat, with many spores, and alkalinity was used as evidence of penicillin production.

3. *Potency Tests:* The broth of each flask was then titrated by the turbidimetric method,[7] since the amount of active principle of these cultures is not always the same. Standard cultures of *Staphylococcus aureus* and *Streptococcus hemolyticus*[8] were used as the test strains. Purified penicillin* containing 102 Oxford units per mg.[9] was used as a standard to determine the number of units of penicillin in the crude preparation. The test was performed by making serial dilutions of both types of penicillin in 10 Ml. of beef heart infusion of broth as follows: 1:50, 1:100, 1:500 and 1:1000 in duplicate. Eighteen-hour broth cultures of both test strains were previously adjusted to contain 1×10^7 micro-organisms per Ml. McFarland scale. One-tenth milliliter of this dilution of the staphylococcus was then added to each tube of the first set of dilutions of the two penicillin preparations and the streptococcus to the other set. Failure to develop turbidity after 18 hours incubation at 37° C. was accepted as evidence of inhibition. Inhibitory action was determined by the least amount of penicillin necessary to inhibit the growth of the inoculum. It was found that our preparation usually contained approximately 800 units per Ml.

4. After potency tests were read, the broth of those flasks showing at least 500 units per Ml. were pooled and the reaction was then adjusted to approximately p_H 6.8 with 3 per cent HCl, using phenol red as the indicator.

5. The broth was then filtered through a W. 'Berkfeld' filter and the filtrate (penicillin) was then retested for potency and also for sterility.

6. Sterility tests were performed by using the same dilutions of penicillin as for potency tests; these dilutions were inoculated into a duplicate set of tubes containing 10 Ml. each of dextrose broth, glucose semisolid broth and in beef heart broth. One set of these tubes was incubated aerobically and the other set was incubated anaerobically at 37° C. for 48 hours. If there was no evidence of growth the penicillin was considered sterile and safe for clinical use. This crude penicillin, when stored in the refrigerator, maintained its potency for six to eight weeks.

7. Sensitivity tests on the micro-organism isolated from the patient is also performed by the method described in the first paragraph under *"Potency Tests."* This is especially important, as some of the staphylococci and streptococci are resistant to penicillin.

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* Purified penicillin was supplied by Merck & Co.

8. The mats of *Penicillium notatum* were saved in the original flasks for a period of one week and gauze dressings inoculated with them as needed.

CLINICAL USE

This crude penicillin preparation was used as nose and throat drops and for local application on a tracheotomy wound on a ten-month-old infant (M.F.) This patient, when admitted to the hospital, was acutely ill and had almost complete stenosis due to subglottic edema and thick green exudate on the cords as revealed by laryngoscopy. Cultures from the nose, throat and larynx revealed *hemolytic Staphylococcus aureus.*

Sulfadiazine and steam treatment were given, but the patient's condition grew worse, and five hours after admission a tracheotomy was performed, with complete relief of symptoms. Two days after tracheotomy the patient again developed severe respiratory distress and a bronchoscopy was performed. Aspiration of a waxy mucus plug gave complete relief of symptoms.

Sulfathiazole was then used because of continued temperature and the crude penicillin was applied as nose and throat drops four times a day. The condition of the patient gradually improved, chemotherapy and penicillin were discontinued after the third day of treatment. The tracheotomy wound, however, became infected with the *Staphylococcus aureus* three days after the operation. Sulfathiazole powder, which had been applied to the wound, was ineffectual, and the edges of the wound were necrotic, with a profuse discharge of thick green pus. When the tracheotomy tube was removed six days postoperatively, attempts to close the wound were unsuccessful. Local application of the crude penicillin, 20 drops every hour on the open wound, was begun after the sulfathiazole powder was discontinued. Within three days the wound showed healthy granulation, with a small amount of thin discharge.

After nine days of penicillin treatment the wound was completely healed, leaving a smooth scar. Roentgenologic examination showed only slight compression of the trachea.

Two other patients were treated with this type of penicillin. They had severe pharyngitis caused by *Staphylococcus aureus.* One, C. W., a six-year-old male Negro, was admitted to our diphtheria service with a five-day history of illness. The child had a temperature of 104.8° F. and was in a comatose state. Examination revealed a membranous tonsillitis, cervical adenitis and a "bull-neck," suggestive of diphtheria. Bacterial examination of nose, throat and larynx revealed *Staphylococcus aureus* in pure culture. Sulfadiazine was administered for the first 48 hours after admission, but had to be discontinued because of oliguria. The condition of the throat remained unchanged. Crude penicillin was then applied by means of a swab directly on the tonsils and pharynx every three hours for three days and four times a day thereafter for three days. On the third day of treatment there were

only small patches of exudate on the tonsils and pharynx, and at the end of seven days there was complete clinical recovery.

The third patient treated with penicillin was a five-and one-half-year-old white male, R. C., who presented the same clinical picture as C. W. He was admitted to our diphtheria service on the fourth day of illness. A cheesy, necrotic, thick membrane was seen in his pharynx and throat. Cervical adenitis was also present but not as marked as in C. W. Sulfadiazine was given for four days. Penicillin was administered on the second day after admission in the same manner as for C. W. The bacteriologic examination revealed *Staphylococcus aureus* in throat and larynx. The temperature, which was 103.6° F. on admission, dropped to normal on the third day of treatment. The throat was clinically improved three days after penicillin treatment was begun and was completely normal five days after the beginning of the treatment.

These cases illustrate the use of local application of the crude penicillin, which is prepared in our hospital laboratory. This preparation was extremely efficacious in clearing nose and throat infections as well as a tracheotomy wound infected with *hemolytic Staphylococcus aureus*.

ADDENDUM

Since this paper was submitted a case of surgical scarlet fever was treated successfully with both gauze dressings inoculated with *Penicillium notatum* and crude penicillin filtrates. A critically ill, eight-year-old white female was admitted to the varicella service on the third day of illness, with a temperature of 106° F. She had a history of a streptococcus infection of the left hand 19 days before admission. The varicella lesions on the abdomen were infected and an extensive cellulitis, extending up the sides to the line of the nipple and down to the midthighs, was present. Cultures from the infected lesions showed hemolytic streptococcus. The inoculated gauze dressings were placed over the entire abdomen and were kept moist with the crude penicillin diluted to contain 200 units per Ml. The treatment was continued for ten days. The cellulitis began to subside after the third day of treatment and on the fifth day there was only a small area, 3 x 3 inches, which was indurated. On the tenth day all the lesions were healed and there was very little scarring. During local penicillin applications she was also given sulfadiazine, seven grains every four hours. A younger sister of this patient, admitted to the hospital two weeks previously, had the same type of infected varicella lesions and cellulitis of the abdomen. She received only sulfadiazine. The infection localized in the right inguinal area, necessitating surgical intervention. The wound is still draining, two weeks after the operation.

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POSTOPERATIVE CHRONIC PROGRESSIVE GANGRENE OF THE ABDOMINAL WALL

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THE PURPOSE of this paper is to report a case of postoperative chronic progressive gangrene of the abdominal wall, to point out its characteristic features and to differentiate it clearly from the chronic undermining ulcer as described by Meleney.[1] Meleney[2] reviewed the literature up to 1933 and, though there were a number of cases reported, it was believed that many have been lost in the literature because of inadequate titles. In a more recent review of the literature[3] less than 90 cases were found.

Postoperative gangrene should be differentiated from other chronic gangrenous lesions of the skin, namely gangrenous impetigo, fusospirochetal gangrene, and amebic infection, with gangrene.[2] Gangrenous impetigo appears in undernourished individuals of any age-group who are frequently suffering from recurrent attacks of dysentery. The lesion may be found any place on the body, although the scalp, face, and abdomen are affected most frequently. Small vesicles surrounded by a red zone appear first and, subsequently, the center becomes dark, gangrenous, and depressed. The lesions gradually increase in size and may coalesce, although one to two centimeters is usually the largest size. The disease is contagious. Fusospirochetal gangrene is found in human bites. Inflammation occurs early and this is soon followed by a foul-smelling exudate. The margins of the wound are dark grey-green in color. The infection spreads to the adjoining bones and joints, burrows to the underlying structures, and may produce multiple draining sinuses at a distance. Amebic infection of the skin, with gangrene, usually occurs after a period of days or weeks following the spontaneous or operative drainage of a liver abscess. The edges of the wound are indurated, raised, and dark brown. As the necrosis spreads the center of the lesion remains ulcerated and covered with granulation tissue. The surface contains a foul-smelling exudate of thick, brownish, blood-tinged pus.

CASE REPORT

E. G., white, female, age 69, married, was admitted to the University Hospital from another institution, September 3, 1942, with a previous diagnosis of a postoperative wound infection.

Past History: On July 14, 1942, through a McBurney incision, an appendiceal mass was found. Sulfathiazole (7 Gm.) was placed about the inflammatory mass and the incision was closed, with one cigarette drain. On the fourth postoperative day acute

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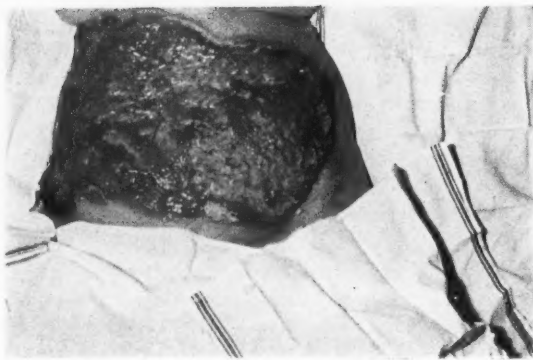s at
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FIG. 1.—Postoperative chronic progressive gangrene of the abdominal wall. This photograph was taken September 23, 1942. Drainage of the appendiceal mass was performed July 14, 1942. The ulcer extends from the pectoral to the pubic region and laterally to the back. Note (1) area of gangrene, (2) area of purplish color, (3) advancing outer zone which is a brilliant red, and (4) the normal zone. The granulation tissue is extensive; there is much purulent material. The right rectus muscle is partially destroyed. (See Figure 2).
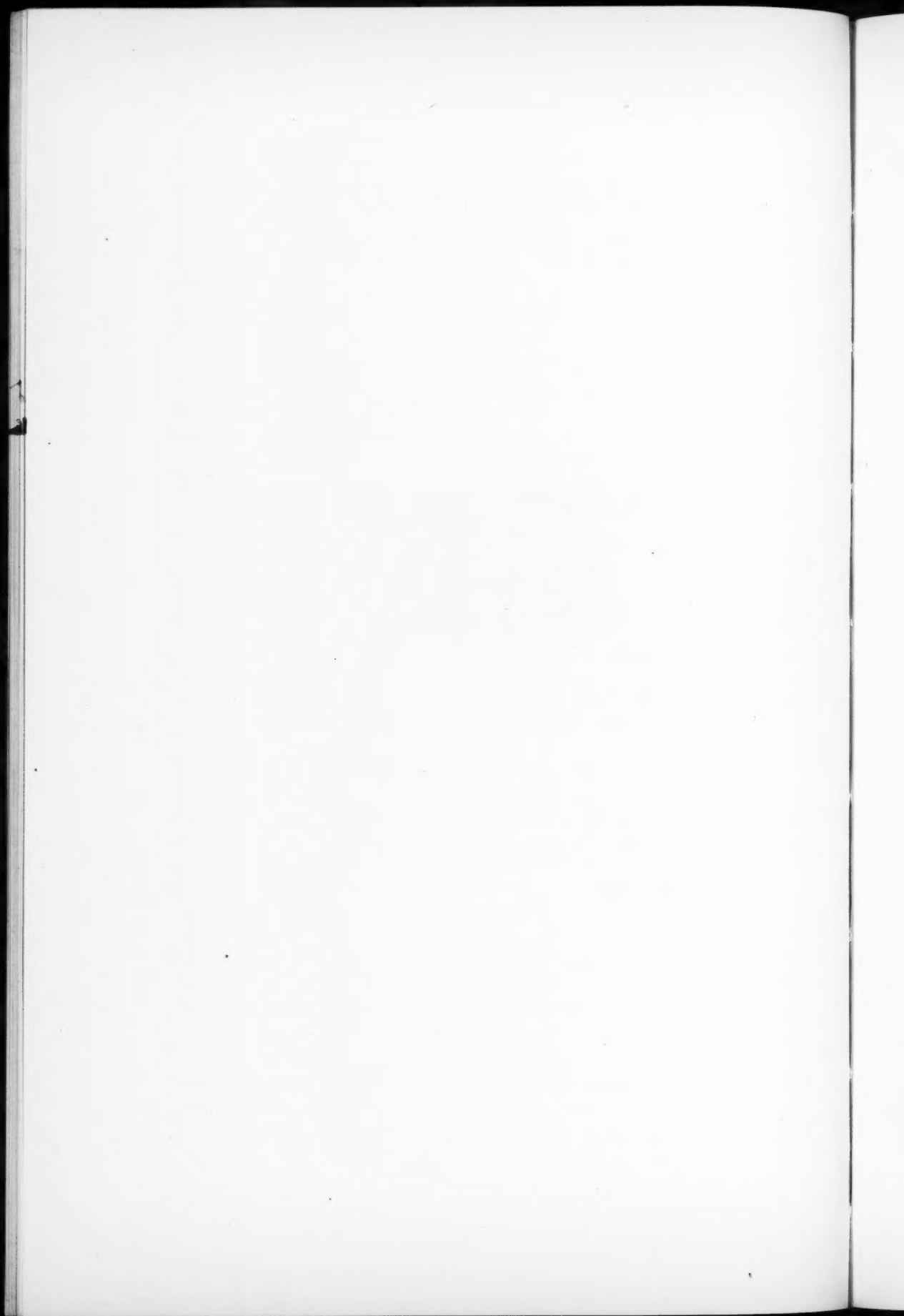
surgical parotitis occurred. This subsided in a few days under roentgenotherapy. On the tenth postoperative day the drain was removed and there was a moderate amount of purulent drainage from the wound. By the 14th postoperative day, the infection had spread to the skin and subcutaneous tissues.

The patient was admitted to the University Hospital on her 51st postoperative day. At this time, the physical examination revealed an elderly, white, emaciated, almost moribund female complaining of severe pain in an ulcerated area around the region of a McBurney incision. The entire abdominal wall was replaced by an ulcer, the base of which was composed of areas of suppuration and granulation tissue, overlaid in some areas with both old and recent blood clots. The rectus muscle was bare in the right lower quadrant. No sinus was found at the wound site leading into the abdominal cavity. The margins of the ulcer were composed of overhanging gangrenous brown skin which, in turn, was surrounded by a purple area about 1.5 cm. in width, which was not undermined. This purplish area of skin merged into a red area about 1 cm. in width, which shaded off into normal skin (Fig. 1).

Moderate pitting edema of the feet was present. There were no other significant findings. Rectal temperature 99.6° F. Hemoglobin 10 Gm. per cent (Sahli). Red blood cells 3,470,000; white cells 14,400. There were no significant findings in the urine. The Wassermann serologic reaction was negative.

Material cultured from various areas of the base and margin of the ulcer revealed *Staphylococcus aureus,* which grew both aerobically and anaerobically, and *B. coli.*

Because the patient was so critically ill, excision of the gangrenous border and adjacent normal skin was delayed. However, the overhanging gangrenous skin edge was débrided and the base of the ulcer irrigated with normal saline solution. Activated zinc peroxide was applied locally only on an empirical basis, with no resulting diminution in the spread of the lesion or change in its characteristics. Blood transfusions were given to replace serum protein loss and to combat anemia. Under this regimen the patient's general condition gradually improved.

On October 26, 1942, the patient's general condition had improved sufficiently to permit administration of a general anesthetic. By this time the base of the ulcer had become relatively clean but the ulcer margin had progressed to the chest wall up to the level of the fourth costal cartilage and around the right flank almost to the midline posteriorly. Material cultured from the ulcer revealed only *Staphylococcus aureus,* which grew both aerobically and anaerobically.

Under nitrous oxide anesthesia, the upper and lateral borders of the ulcer were excised beyond the red zone so as to include normal tissue. Microscopic examination of this tissue revealed nonspecific chronic inflammation and no undermining of viable skin (Fig. 2). About 8 Gm. of sulfathiazole crystals were sprinkled over the whole ulcer base, and warm, moist dressings applied. These dressings were changed daily. A blood level of 12 mg. per cent was obtained, due to local absorption of the sulfathiazole. A secondary *B. pyocyaneus* infection was controlled by daily irrigations with 2.5 per cent acetic acid.

Under this regimen the border at the site of excision remained stationary and began to epithelize in a few places. Because the base of the ulcer remained infected, skin grafting was not considered at this time.

The patient expired December 5th, 1942 (the 144th postoperative day). Final clinical diagnosis was: (1) Postoperative chronic progressive gangrene of the abdominal wall; (2) cachexia; and (3) exhaustion syndrome.

At autopsy the gross pathologic findings consisted of the ulcer involving the whole anterior abdominal wall extending up to the level of the fourth costal cartilage and under the right breast, down over the iliac crests for about 5 cm. beyond the inguinal ligaments and posteriorly around the right flank to the midline. The base of the ulcer in the right lower quadrant was formed of thickened peritoneum. No sinus was

found leading from the peritoneal cavity. The appendix was bound down to the cecum and terminal ileum by fibrous adhesions. No periappendiceal abscess was present.

COMMENT.—Because the treatment of chronic progressive gangrene and chronic undermining ulcers (Meleney) is so different, it is imperative to distinguish them immediately. The diagnosis can be made clinically. Meleney[2] described the early lesions of chronic progressive postoperative synergistic
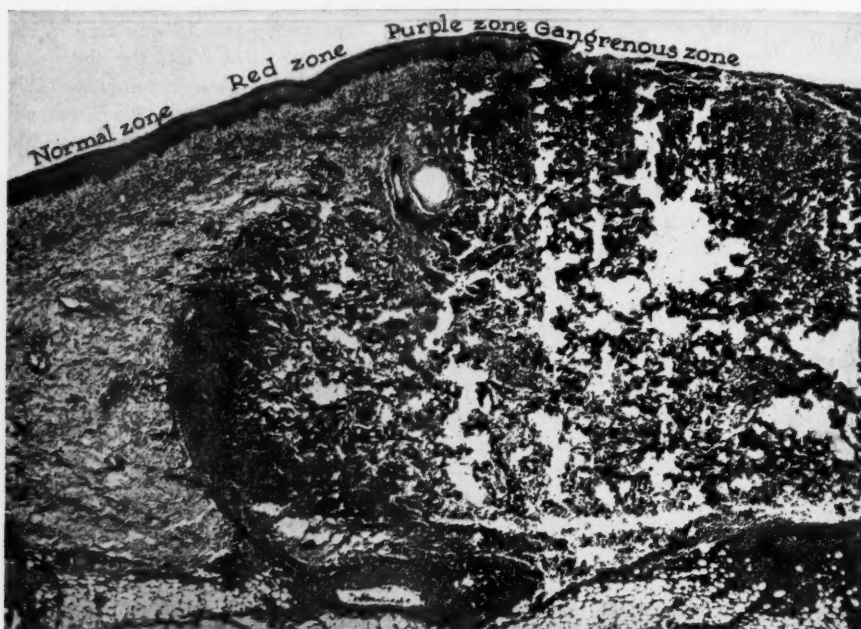

FIG. 2.—Dr. Ruth Balkin. Biopsy from margin of ulcer:

In the *gangrenous zone* (most of the gangrenous skin previously débrided), the tissue is completely necrotic and only degenerating polymorphonuclear leukocytes and round cells and a few hyalinized connective tissue fibers are seen. The necrosis extends down to the subcutaneous fat tissue. At this point there is a sharp line of demarcation formed by newly proliferated capillaries and small numbers of fibroblasts. This granulation tissue as well as the underlying fat is infiltrated with polymorphonuclear leukocytes and round cells, which diminish in number toward the deeper portions of the fat tissue.

The *purple zone* is characterized by the presence of large numbers of polymorphonuclear leukocytes and a few round cells. There are still a few recognizable collagenous connective tissue fibers in the dermis and the overlying epidermis remains intact. Cultures should be made from the purple zone for the *hemolytic Staphylococcus aureus*.

In the *red zone* there is granulation tissue similar to and continuous with that seen above the fat tissue in the purple and gangrenous zones. Cultures should be made from the underlying tissue in the red zone for *microaerophilic nonhemolytic streptococcus*. Beyond this granulation tissue the capillaries are dilated and there are small infiltrations of cells consisting mostly of the large and small mononuclear cells and a few polymorphonuclear leukocytes. These cellular infiltrations are for the most part perivascular. Note that the purple and red zones are raised above the level of the normal skin. (× 25) (See Figure 1.)

bacterial gangrene as follows: "It usually begins to appear about the end of the first or second week after operation, either as an infection of the whole wound or as a localized induration about retention sutures. At first the wound becomes red, swollen, and tender. Within the next few days the wound margins or the stitch holes develop a carbunculoid indurated appearance. The center of activity becomes purplish in color, while the outer zone takes on a brilliant red tint. The whole region becomes exquisitely

tender. *This symptom is an outstanding feature of the disease.* Within a few days the purplish areas become frankly gangrenous. The color of the dead skin changes to a dirty greyish-brown and the surface is dull, like suede leather." As soon as the diagnosis is made clinically (Table I) treatment should be instituted. The treatment should not be delayed for the bacteriologic studies, which require expert technic not generally available.

TABLE I

DIFFERENTIATION OF POSTOPERATIVE CHRONIC PROGRESSIVE GANGRENE AND
CHRONIC UNDERMINING ULCER (MELENEY)

	Postoperative Chronic Progressive Gangrene	Chronic Undermining Ulcer (Meleney)
Age-Group	Usually older individuals (last decades)	Any age-group
Etiology	Usually follows drainage of deep abscesses	Usually after incision and drainage of superficial suppurative processes
Usual Site	(1) Abdominal wall (right lower quadrant) (2) Chest wall	Any part of body
Bacteriology	Synergistic action of: (1) *Microaerophilic nonhemolytic Streptococcus* (2) *Hemolytic Staphylococcus aureus*	*Microaerophilic hemolytic Streptococcus*
Clinical Appearance	Zone 1—Gangrenous overhanging margin Zone 2—Purple area becoming gangrenous (not undermined) where *hemolytic Staphylococcus aureus* may be found Zone 3—Red inflammatory area (advancing zone where *microaerophilic nonhemolytic Streptococcus* is most frequently found). Zone 4—Normal tissue	Undermined skin margin, which frequently may be inverted No gangrene Sinuses and daughter ulcers may be present
Spread of Ulcer	More rapid	Less rapid
Systemic Reaction	Slight	Variable
Local Reaction	Excruciating pain	Slight pain
Local Treatment	Immediate excision beyond red zone including normal zone Sulfonamides locally (?) Skin graft	Activated zinc peroxide and excision of undermined margin; if necessary, skin graft
Prognosis	Good, if active treatment is undertaken early	Good, if active treatment is undertaken early

In debilitated elderly individuals in whom an operation for drainage of an empyema or peritoneal abscess is to be performed, the possibility of postoperative chronic progressive gangrene of the skin should be kept in mind. Under such circumstances, suturing of the wound may predispose to this complication. During the postoperative period, the wound should be observed carefully and at the earliest sign of gangrene, the entire border, including normal skin, should be excised. Sulfonamides may be applied locally, although in our experience these drugs were of no value. After the infection is controlled and healthy granulation tissue is obtained, skin grafts may be applied to the ulcer.

SUMMARY AND CONCLUSIONS

An unusual case of extensive postoperative chronic progressive gangrene of the abdominal wall was observed. This may follow drainage of a deep abscess in either the peritoneal or pleural cavities, especially in older individuals where the wound has been sutured. Treatment consists of early wide excision of the ulcer margin, including normal tissue, replacement of

lost proteins from the gangrenous area and general supportive measures. Local applications of activated zinc peroxide or sulfonamides were of no value in this case.

Postoperative chronic progressive gangrene should be differentiated from a chronic undermining ulcer (Meleney) on a clinical basis by the gangrenous border and lack of undermining, and on a bacteriologic basis by isolation of the *microaerophilic nonhemolytic Streptococcus and hemolytic Staphylococcus aureus.*

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ANNOUNCEMENT

THE SAMUEL D. GROSS PRIZE

The Philadelphia Academy of Surgery has announced that competition is now open for the Samuel D. Gross Prize of $1500. Essays will be received until January 1, 1945. The Committee members are Charles F. Mitchell, M.D., Calvin M. Smyth, M.D., and Damon B. Pfeiffer, M.D.

The conditions annexed by the testator are that the prize "shall be awarded every five years to the writer of the best original essay not exceeding one hundred and fifty printed pages, octavo, in length, illustrative of some subject in Surgical Pathology or Surgical Practice founded upon original investigations, the candidates for the prize to be American citizens."

It is expressly stipulated that the competitor who receives the prize shall publish his essay in book form, and that he shall deposit one copy of the work in the Samuel D. Gross Library of the Philadelphia Academy of Surgery, and that on the title page it shall be stated that to the essay was awarded the Samuel D. Gross Prize of the Philadelphia Academy of Surgery.

The essays, which must be written by a single author in the English language, should be sent to the "Trustees of the Samuel D. Gross Prize of the Philadelphia Academy of Surgery, care of the College of Physicians, 19 South 22nd Street, Philadelphia," on or before January 1, 1945.

Each essay must be typewritten, distinguished by a motto, and accompanied by a sealed envelope bearing the same motto, containing the name and address of the writer. No envelope will be opened except that which accompanies the successful essay. The Committee will return the unsuccessful essays if reclaimed by their respective writers, or their agents, within one year. The Committee reserves the right to make no award if the essays submitted are not considered worthy of the prize.